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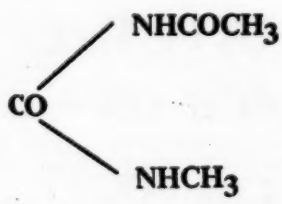

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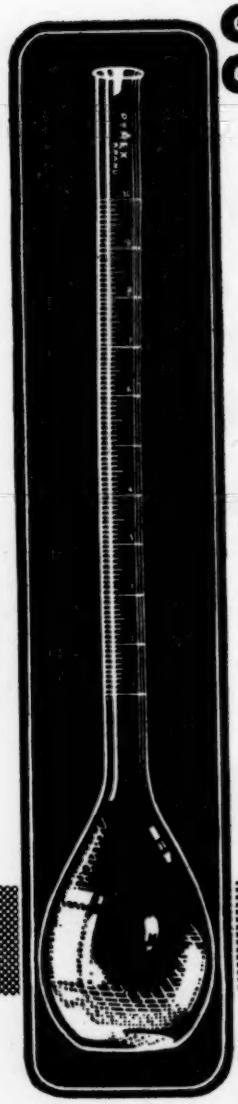

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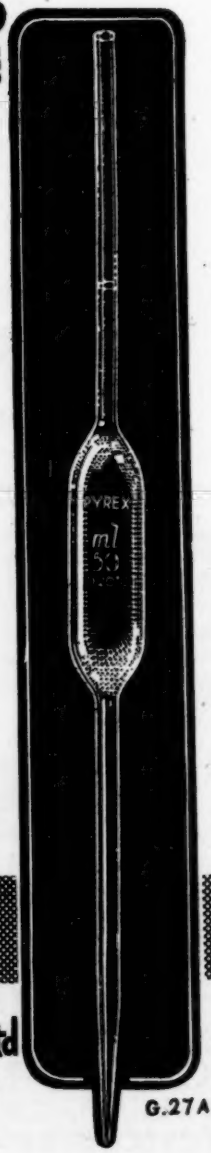

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ERRATA.

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Page	Line	
591	Formula VI.	*Attach a minus sign to the upper oxygen atom.*
613	21*	*For* "$C_{22}H_{32}O_4N_4S$" *read* "$C_{24}H_{32}O_2N_4S_2$."
614	8	*For* "$C_{20}H_{24}ON_2$" *read* "$C_{20}H_{24}N_4.2HCl,2H_2O$."

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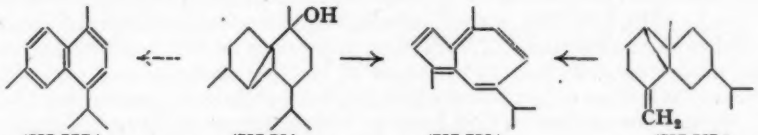
191	18*	*After* "methanol–hot water" *insert* "forming flat needles, m. p. 184—188°."

* From bottom.

azulene and relatively little cadalene. A similar case is afforded by aromadendrene (XLVI) (Radcliffe and Short, J., 1938, 1200; Naves and Perrottet, *Helv. Chim. Acta*, 1940, **23**, 912), which is dehydrogenated to give guaiacazulene and not a derivative of naphthalene.



(XLIII.) (XLV.) (XLIV.) (XLVI.)

" *Diphenylene.*"—Diphenylene (also called biphenylene and *cyclo*butadibenzene) is the tricyclic hydrocarbon (XLVII), isomeric with acenaphthylene, which has been regarded for a long time as a possible aromatic type. Five arrangements of the bonds are possible, four dibenzenoid in character, and one doubly ortho-quinonoid.

The hydrocarbon has an interesting history. Hosaeus in 1893 (*Monatsh.*, **14**, 323) attempted to prepare it by the action of sodium on *o*-dibromobenzene, but obtained instead a trace of benzene, a little diphenyl and a mixture of complex products. Niementowski (*Ber.*, 1901, **34**, 3331) treated the diazonium salt derived from 2 : 2′-diaminodiphenyl with copper powder, but the product was carbazole. The dehydration of 2-hydroxydiphenyl to diphenylene was unsuccessfully attempted by Cullinane, Morgan, and Plummer (*Rec. Trav. chim.*, 1937, **56**, 627). The preparation of diphenylene from 2 : 2′-dibromodiphenyl in almost theoretical amount by the action of sodium in boiling ether was claimed by Dobbie, Fox, and Gauge (J., 1911, **99**, 683; 1913, **103**, 36). It was described as closely resembling diphenyl but had a higher melting point (74·5—75°; diphenyl, 70·5°); it was extremely volatile and concordant results for the analyses were only obtained by carrying out the combustions under abnormally vigorous conditions. The three selected analyses and the molecular weight determinations are in fair agreement with the formula $C_{12}H_8$. The hydrocarbon was not attacked by cold alkaline permanganate, but hot chromic acid mixture gave phthalic and benzoic acids. Bromination gave 2 : 2′-dibromodiphenyl and a dibromodiphenylene giving *p*-bromobenzoic acid on oxidation. The nature of this hydrocarbon remains obscure, and its preparation has not been successfully repeated in spite of many attempts. Complete failure has been reported by Mascarelli and Gatti (*Gazzetta*, 1933, **63**, 661), by Rapson and Shuttleworth (J., 1941, 487), and by Lothrop (*J. Amer. Chem. Soc.*, 1941, **63**, 1187), although a variety of experimental conditions was used, including the replacement of sodium by potassium, and the dibromodiphenyl by the corresponding dichloro- and di-iodo-derivatives.

(XLVII.) (XLVIII.) (XLIX.) (L.) (LI.)

Lothrop (*loc. cit.*), having failed to repeat the earlier claim, finally succeeded in preparing a compound $C_{12}H_8$ in 5% yield by distilling 2 : 2′-dibromodiphenyl or, better, 2 : 2′-di-iododiphenyl with cuprous oxide, steam-distilling the product, and purifying the substance as its scarlet picrate. The hydrocarbon was finally liberated from the picrate by sublimation at 100°, and obtained in light-yellow prisms, m. p. 110°, which was shown by analysis and molecular weight determination to be undoubtedly $C_{12}H_8$. The substance is not identical with the compound described in 1911, nor with acenaphthylene, and is claimed by Lothrop as diphenylene (XLVII). Oxidation with chromic acid gave some phthalic acid (yield unstated), and by passage as a vapour with hydrogen over hot copper it was one-third converted into diphenyl and two-thirds unchanged. The stability and colour of its picrate are consistent with a tricyclic aromatic hydrocarbon (see Basil and Hauber, *J. Amer. Chem. Soc.*, 1931, **53**, 1090), as is also its absorption spectrum (Carr, Pickett, and Voris, *ibid.*, 1941, **63**, 3231). Lothrop also brought forward evidence in favour of the symmetrical structure of the molecule. 2 : 2′-Di-iodo-4 : 4′-dimethyldiphenyl (XLVIII) and 2 : 2′-di-iodo-5 : 5′-dimethyldiphenyl (L) were each converted into a " diphenylene," and the products from both reactions were identical, being regarded as 2 : 7-dimethyldiphenylene (XLIX). A later paper by the same author (*J. Amer. Chem. Soc.*, 1942, **64**, 1698) described two other diphenylenes, the 1 : 8-dimethyl- and the 2 : 7-dimethoxy-derivatives.

Two novel features are involved in the diphenylene formulæ for these compounds. First, they may be regarded as derivatives of the unknown substance *cyclo*butadiene, and secondly they contain a four-membered ring fused to a benzene nucleus. With regard to the first point there is evidence to suggest that the *cyclo*butadiene ring may be stabilised by fusion with the benzene nuclei. The second point is more difficult, because there appears to be no established case in chemical literature of a compound containing fused aromatic and four-membered rings, a subject which is discussed in a separate section (p. 266). Such molecules would have bonds attached to the aromatic nucleus strained through angles of 30°; in the case of diphenylene (XLVII) four bonds would be strained to this large extent and it might be expected that the resulting strain would confer a considerable degree of instability upon the molecule, whereas the actual " diphenylenes " are very stable, being formed by high temperature reactions, and behaving as typical aromatic compounds.

The preparation of the hydrocarbon $C_{12}H_8$ by Lothrop's method has been confirmed (Baker, Grice, and Donne, unpublished observations; Baker, *Nature*, 1942, **150**, 210) and it was reported that mild catalytic

reduction resulted in the uptake of approximately three molecules of hydrogen, giving a volatile oil, and that it behaved as a saturated compound and exhibited no acetylenic properties. The same hydrocarbon has also been prepared in 4% yield by Rapson, Shuttleworth, and Niekerk (*loc. cit.*; Rapson and Shuttleworth, *loc. cit.*) by treating the Grignard reagent prepared from 2 : 2′-dibromodiphenyl with dry cupric chloride (method due to Krizewsky and Turner, J., 1919, **115**, 560), a reaction which simultaneously yields tetraphenylene (see p. 261).

Apart from the diphenylene structure (XLVII) there appears to be only one alternative for a hydrocarbon $C_{12}H_8$ possessing the properties described and capable of yielding phthalic acid on oxidation. This is the structure (LI), the benzo-derivative of pentalene which has been called *cyclo*pentindene (Patterson and Capell, "The Ring Index," 1940). The suggestion that Lothrop's diphenylene might be *cyclo*pentindene was made in 1942 (Baker, *loc. cit.*), thus avoiding the two difficulties inherent in the diphenylene formula which have already been mentioned. On general grounds (LI), for which three arrangements of the bonds are possible, two benzenoid and one ortho-quinonoid, would be expected to be a stable, almost strainless molecule of aromatic type. Coulson (*Nature*, 1942, **150**, 577) has calculated that the resonance energies of diphenylene and *cyclo*pentindene differ by only about 4 kg.-cals., the former being the greater, but that diphenylene possesses a strain energy of possibly 100 kg.-cals., whereas the strain energy of *cyclo*pentindene is only a few kg.-cals., and concludes that *cyclo*pentindene should be considerably more stable than diphenylene.

At the time when the *cyclo*pentindene structure was put forward as an alternative to the diphenylene formula all the known facts were capable of explanation on the basis of either structure. Even the production of the same dimethyl derivative from structurally isomeric di-iododiphenyls may be accounted for by assuming that under the vigorous conditions of the reaction one of the benzene rings undergoes rupture at the bond common to the benzene and the four-membered ring (Baker, *loc. cit.*). More recently, however, three pieces of evidence have become available which give strong support to the diphenylene structure. Waser and Schomaker (*J. Amer. Chem. Soc.*, 1943, **65**, 1451), in an electron diffraction investigation of diphenylene, find inter-atomic distances of 1·42 A. (very strong), 2·44 A. (strong), 2·78 A. (strong), corresponding to the average bonded C–C distances, the *meta*- and *para*-distances in the benzene ring respectively, and 2·1 A. (very weak) regarded as the diagonals of the four-membered ring. These authors state that the *cyclo*pentindene structure is definitely excluded, because there are no C–C distances of 2·30 A. corresponding to the calculated diagonals of two regular pentagons. The validity of this assertion rests upon assumptions as to the dimensions of the two five-membered rings. These will not be regular, because, for example, the bond common to the two is wholly single, so that some of the diagonals may equal the distance between *meta*-carbon atoms in the benzene ring. The absence of any indication of a distance of the order of 2·30 A. is, however, scarcely consistent with the *cyclo*pentindene structure. A preliminary note of an incomplete *X*-ray crystallographical investigation of Lothrop's hydrocarbon by Chia-Si Lu (included in the paper by Waser and Schomaker, *loc. cit.*) shows a complex unit cell containing six molecules. Provisionally it has been suggested that two of these molecules may have a centre of symmetry, but this evidence has yet to be confirmed.*

The third piece of evidence concerns the reduction of diphenylene. It was suggested by Baker (*loc. cit.*) that a molecule possessing the diphenylene structure should undergo ready catalytic reduction with rupture of the strained four-membered ring to give diphenyl, and it was stated that in fact the compound combines with approximately three molecules of hydrogen. This statement was based on catalytic reduction experiments in acetic acid at room temperature in presence of a palladium–charcoal catalyst, and these experiments have since been confirmed. It has been found, however (unpublished experiments), that the course of the reduction is quite different when hydrogenation is effected in alcoholic solution in presence of Raney nickel; the uptake of hydrogen is rapid and ceases after little more than one molecule of hydrogen is absorbed, and an 85% yield of pure diphenyl can be isolated from the product. It is difficult to imagine how *cyclo*pentindene could so readily yield diphenyl, as the reaction involves the breaking of two presumably strainless C–C links and the formation of a new C–C link.

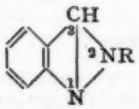
The balance of evidence is thus definitely in favour of the original diphenylene structure for Lothrop's hydrocarbon. If future work confirms this conclusion, diphenylene will have to be regarded as a unique type of molecule, in which the butadiene structure is stabilised by fusion with the two benzene rings, just as the *cyclo*octatetraene structure may be stabilised by fusion with three or four benzene rings, and in which the expected instability due to strain is compensated by increased stability due to resonance. It is probably also the only type of molecule in which it is possible to have an aromatic nucleus fused to a four-membered ring.

Non-existence of Compounds containing a Four-membered Ring fused to an Aromatic Nucleus.—Many formulæ are to be found in chemical literature in which an aromatic nucleus is shown fused to a four-membered ring. These fall broadly into three types, (1) tricyclic benzenoid compounds such as anthracene, acridine, phenazine, etc., (2) bicyclic compounds containing nitrogen with a bridged five-membered ring fused to a benzene ring, such as anthranil, 2-alkylindazoles, etc., and (3) a number of compounds of quite unrelated types. It would not be profitable to discuss individual cases in the last category; most of the suggested four-membered ring structures are advanced without experimental justification, and in some cases the work is of doubtful value and a knowledge of the molecular weight of the compound is lacking. Sometimes a dipolar molecule is represented as completely covalent, and in one instance the four-membered ring is only made possible by the

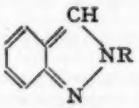
* Note added, April 30th, 1945. The complete *X*-ray crystallographical analysis of diphenylene has now become available (Waser and Chia-Si Lu, *J. Amer. Chem. Soc.*, 1944, **66**, 2035). The results establish conclusively the structure of the compound as (XLVII).

inclusion in the formula of two quinquevalent carbon atoms. In all these cases the onus of proof rests with those who suggest the formulæ.

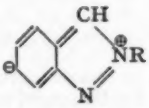
(LII.)



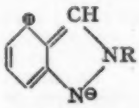
(LIII.)



(LIV.)



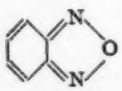
(LV.)



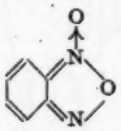
(LVI.)

With regard to type (1), anthracene, acridine, and related molecules were at one time written with long covalent links joining the central atoms of the system, thus making two four-membered rings as in (LII). The *X*-ray investigation of anthracene crystals by Robertson (*Proc. Roy. Soc.*, 1933, *A*, **140**, 79) has shown that the three hexagons are completely regular, so that the central atoms cannot be covalently linked. Further evidence on this point is that if the structure of anthracene were (LII), then its resonance energy would be simply that due to the two isolated benzene rings, namely $2 \times 39 = 78$ kg.-cals., whereas it is actually but little less than three times the value for benzene, namely, 105 kg.-cals. These molecules are clearly hybrid and may be written with four arrangements of the double bonds corresponding to the most stable structures which contribute to the normal state of the molecule (see Pauling, "The Nature of the Chemical Bond," Cornell University Press, 1939). It has thus rightly become customary to write these anthracene-like molecules without the central bond.

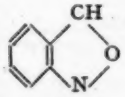
Bicyclic compounds of type (2) have been represented as containing either a four-membered ring as shown in formula (LIII) for a 2-substituted indazole, or else as being ortho-quinonoid in structure as shown in formula (LIV). The 2-alkyl- or 2-aryl-indazoles do not appear to possess the characteristics of genuine ortho-quinonoid compounds, such as colour and ability to add two molecules of bromine, and there can be little doubt that the molecules are resonance hybrids composed of the neutral orthoquinonoid form and not less than thirty-six additional dipolar forms, of which two are shown in formulæ (LV) and (LVI). If for simplicity it is assumed that these dipolar forms all contribute equally to the hybrid, the distribution of the charges is found to be such that the nitrogen atom in position 2 bears a certain positive charge, nitrogen atom 1 and carbon atoms 3 each bear one-fifth, and the six carbon atoms of the benzene nucleus each bear one-tenth of the corresponding negative charge. The result is that the molecule is stabilised by resonance to such an extent that it shows aromatic stability, and there is no need to assume the presence of the four-membered ring. As in the case of anthracene, the real state of the molecule cannot be represented by a single formula, and the determination of the actual resonance energy of such molecules and of the interatomic distances in the five-membered rings would be of very considerable interest.



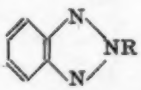
(LVII.)



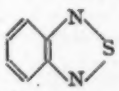
(LVIII.)



(LIX.)



(LX.)



(LXI.)

There is evidence that certain molecules of this kind, all of which possess the same resonance possibilities, are much closer to genuine ortho-quinonoid types than others. This is the case with benzfurazan (LVII) and benzfurazan oxide (LVIII), which were at one time written with four-membered rings. These compounds behave like *o*-quinones in that they combine additively with two molecules of bromine, addition occurring at the olefinic bonds of the six-membered ring, and are, therefore, best represented by the formulæ shown (Hammick, Edwardes, and Steiner, J., 1931, 3308), but the rather slow rate of addition indicates some departure from the fixed ortho-quinonoid structure. The majority of molecules of this type which have been written with four-membered rings are, however, of a more hybrid character; they include anthranil (LIX; in this and the two succeeding formulæ no attempt is made to indicate the distribution of the valency electrons in the five-membered rings, and the benzene nucleus is shown as aromatic), *C*-methylanthranil, and anthranilcarboxylic acid (anthroxanic acid), thioanthranil, 2-substituted benztriazoles (LX), piazthiole (LXI), and piazselenole.

Further evidence which shows that compounds possessing a four-membered ring fused to an aromatic nucleus are at least not easy to prepare is to be found in a study of reactions where such a ring system might be produced. For example, dehydration of salicylic acid does not give a four-membered ring anhydride, but disalicylide containing an eight-membered ring, tetrasalicylide containing a sixteen-membered ring, and polysalicylides; some derivatives of salicylic acid are known to behave similarly. Phenol-*o*-sulphonic acids give not intramolecular but intermolecular anhydrides; anthranilic acid yields only intermolecular amides, and similar cases could be cited. The action of sodium on *o*-xylylene dibromide (Baker, Banks, Lyon, and Mann, J., 1945, 27) gives the centro-symmetric form of 1 : 2 : 4 : 5-dibenz-$\Delta^{1:5}$-*cyclo*octadiene, 1 : 2 : 5 : 6 : 9 : 10-tribenz-$\Delta^{1:5:9}$-*cyclo*dodecatriene, and polymeric products.

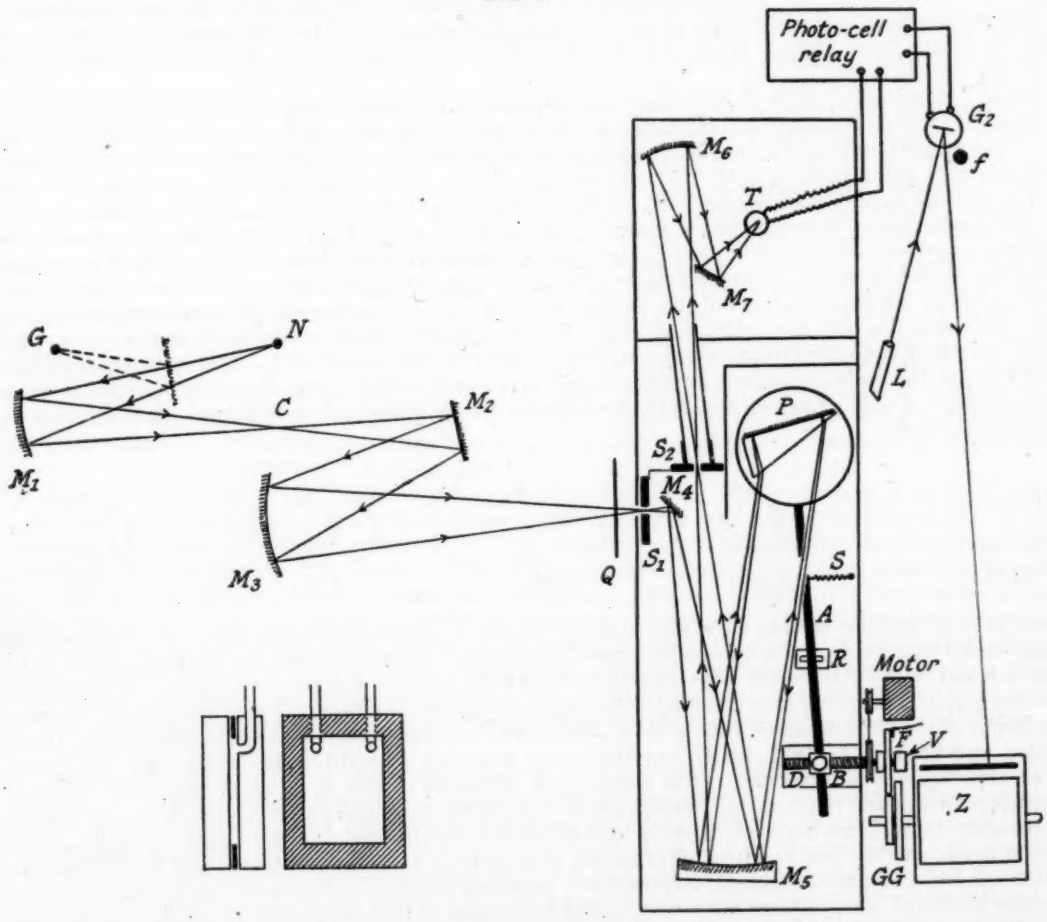
68. *The Infra-red Spectra of Cresols and Xylenols and the Analysis of Cresylic Acid.*

By D. H. Whiffen and H. W. Thompson.

The infra-red spectra of cresols and xylenols have been measured over a wide spectral range. Details have been given of a method for the rapid analysis of cresylic acid, and the basis for similar work on mixtures of xylenols has been explained. Some correlations of the spectra with molecular structure have been outlined, and the effect of the substituent groups on a vibration frequency of benzenoid substances has been considered. The possibility of formulating general rules by which *o*-, *m*-, and *p*-derivatives may be distinguished regardless of the particular substituents has been considered, and similar considerations have been applied to trisubstituted benzenes. A peculiarity in the spectra of some of the phenolic compounds has been discussed in relation to molecular association.

The quantitative analysis of mixtures of *o*-, *m*-, and *p*-cresol by chemical methods is difficult, not very accurate, and unreliable if certain other related substances are also present. A more satisfactory method than those in current use is therefore desirable. We have recently measured the infra-red absorption spectrum of each of these substances over the range of wave-lengths 7—14 μ as part of a general programme on the correlation of vibrational spectra with molecular structure, and also in connexion with similar work on the structure of resins and condensates between phenol or cresol and formaldehyde. It became clear that the infra-red absorption spectrum would provide a quick and simple method for the analysis of cresylic acid. Similar measurements have also been made with xylenols, which form a basis for the analysis of these isomers.

Fig. 1.



Experimental.

The infra-red spectrometer was an automatically recording instrument built in this laboratory and shown diagrammatically in Fig. 1. Although the main optical arrangement is fairly well known, it will be useful for purpose of future reference to describe its main features and dimensions, since it was designed to have high resolving power without being unnecessarily elaborate.

Radiation from a Nernst glower N (or heated Globar rod G) is focused by aluminised mirrors M_1, M_2, M_3 on to the entrance slit of the spectrometer S_1. M_1 and M_2 are concave mirrors of about 60 cm. radius of curvature and about 8 cm. in diameter. M_3 is a plane mirror and the source N (or G) is placed at the centre of curvature of M_1 so as to form a primary image at C, where the absorption cell is usually placed. Mirrors M_2 and M_3 form a second image on S_1. The absorption cell can also be placed just in front of the slit S_1, but with a cell made of a pair of polished rock-salt plates each about 5 mm. thick, a better focus on the slit is obtained with the cell at C, and this is essential if thin solid films of plastics, rubber or other materials with an irregular surface are being studied.

Behind S_1 a small plane mirror M_4 diverts the entrant beam on to the off-axis paraboloid mirror M_5, of focal length 60 cm. A parallel beam of radiation is then directed at the 30° prism P (rock-salt, quartz or potassium bromide) which has a reflecting back face of gold or aluminium. The prism has a reflecting face 10 cm. in length and 60 mm. in height, and is set up in Littrow mounting. After two refractions the beam returns to the mirror M_5 and is thereby focused on the second slit S_2, through which it passes on to M_6 and M_7 and is collected by the Schwarz compensated thermocouple T. The E.M.F. obtained is amplified by a twin photocell relay using a divided Eel selenium cell, a Cambridge d'Arsonval galvanometer of 10 ohms resistance as primary, and a similar galvanometer of higher resistance as secondary. A spot lamp L with line aperture is directed at the secondary galvanometer G_2 and the beam is returned to the camera Z, a cylindrical drum around which the photographic paper is fixed, moving behind a cylindrical lens. With the prism set at a given angle to the beam of radiation from M_5, a definite wave-length returns to the slit S_2 and the energy at this wave-length is recorded by the throw of the galvanometer G_2 from its zero position. As the prism rotates, the galvanometer throw is recorded on the camera, which is geared to the rotatory motion of the prism, both being driven by a D.C. motor. Smooth, slow rotation is obtained by allowing a machined aluminium rod A, supported at R on a ball race and restrained by a light spring S, to be propelled by another circular ball race B fixed to a nut through which the fine screw D is driven. By this mechanism the camera records a curve showing how the energy falls off as a function of increasing wave-length, and simulating the fall-off curve of a black-body radiator. Absorption bands appear as troughs in the background curve and percentage absorption can be calculated by measurement of this photographic trace at desired points. By means of suitable gears GG, the curve may be compressed or spread out along the camera paper.

As the main driving screw rotates, a contact F is made at five equal intervals during each complete revolution of the screw, causing a small filament bulb f near G_2 to flash and produce a line across the camera paper. These lines are calibrated in wave-lengths by reference to the well-established absorption bands of water, ammonia, and other substances. The main drive can be de-clutched and the prism table rapidly brought back to any desired setting, a revolution counter V enabling measurements to be started at the wave-length required.

The main parts of the spectrometer are mounted on steel plates fixed along a length of H girder, and the whole enclosed in a wooden box with loose panels in the top above the slit S_2 and prism P. The thermocouple T is sealed off from the remainder of the instrument in a separate compartment, into which the radiation is led from the slit S_2 through a narrow cylindrical tube fixed around the circumference of the slit mount. It is very desirable to isolate the thermocouple in this way if proper thermal stability is to be obtained.

For the shutter Q, metal, glass, quartz or other materials are used according to the particular spectral range under investigation. For the region 7—14 μ, a quartz shutter being used, the scattered radiation of false wave-length was very small.

The absorption cell was usually made by separating a pair of polished rock-salt plates by a metal washer of the desired thickness and cementing the whole together with a thin film of seccotine. Such cells had a pair of small gaps in the upper edge of the washer for filling and emptying. Since, in the present work, solutions in carbon disulphide had to be used, some form of sealed cell had to be employed. This was achieved by drilling holes about 2 mm. in diameter into one of the rock-salt plates as shown in the diagram. Into these holes were cemented short lengths of copper tubing, and after being filled with the solution the copper tubes were fitted with rubber caps. Such a cell was usually painted around the edges with porcenam cement.

We are particularly indebted for purified samples of the cresols to Bakelite Ltd., for the xylenols to Monsanto Ltd., and to Courtaulds Ltd. Other laboratory specimens were also used. In cases where more than one sample of a given compound was available, the identity of the spectra was a valuable check on purity. The detection of a small amount (1—2%) of *m*-cresol in one sample of 2 : 6-dimethylphenol, and of a trace of unidentified impurity in a sample of 3 : 4-dimethylphenol also served to illustrate the value and power of this analytical method.

The samples of phenol, carbon disulphide, and *cyclo*hexane used were purified commercial products.

Results.—Fig. 2 shows the absorption spectra of the three cresols, obtained from measurements on solutions in carbon disulphide over the range 700—1300 cm.$^{-1}$ (14—7·5 μ). Correlation of all the absorption bands with particular normal vibrational modes must be deferred, but for the present purpose it can be seen that each isomer has an intense absorption band in the region 750—800 cm.$^{-1}$ (12—13 μ), and another region of intense absorption between 1200 and 1300 cm.$^{-1}$. The band in the region 12—13 μ is characteristic of benzenoid substances with substituents attached to the nucleus, and it is almost certainly related to the intense absorption band of benzene at 671 cm.$^{-1}$. The latter has been assigned by Ingold and others (J., 1936, 971) to a motion involving the deformation of C–H bonds out of the plane of the nucleus. There is a shift of this "aromatic" band towards higher frequencies in passing along the series *o*-, *m*-, *p*-, and this seems to occur with most disubstituted benzenes regardless of the particular substituent groups. With *o*-cresol it is found at 750 cm.$^{-1}$, with *m*- at 776 cm.$^{-1}$, and with *p*- at 815 cm.$^{-1}$. The band is so intense with each isomer that it still gives a conveniently large optical density when most of the other bands in the spectrum are feeble, and these are ideal circumstances for infra-red analysis.

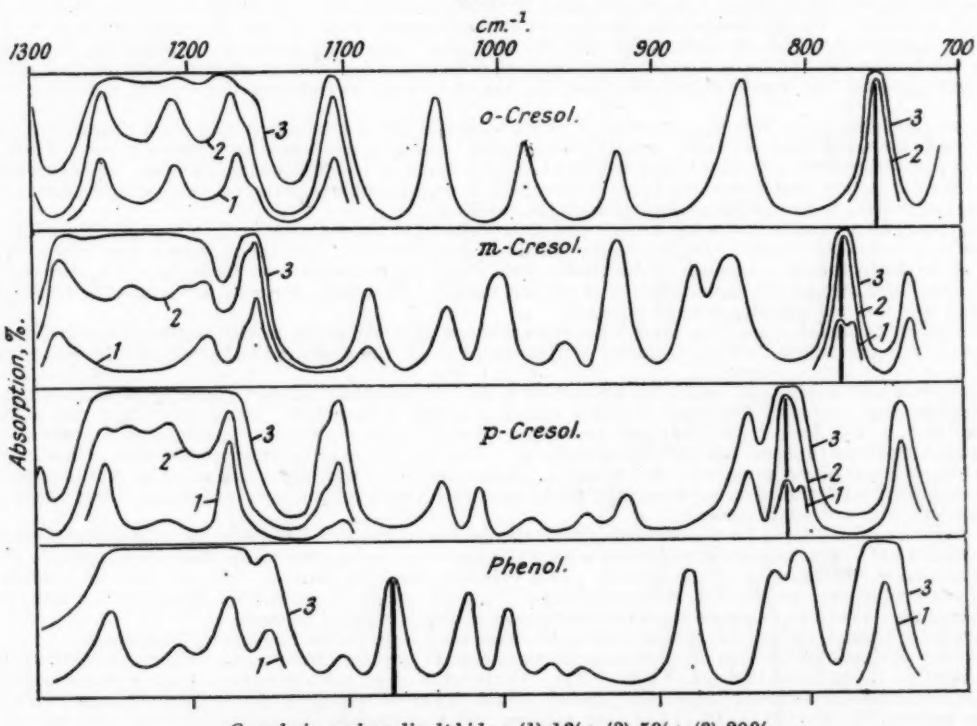
For qualitative analysis, inspection of the spectrum of a mixture at once reveals whether peaks are present at the wave-lengths characteristic for each component. If the usual absorption laws hold, the amount of a component present can then be correlated with the percentage absorption at its key wave-length in the usual way. Thus, for a pure component the extinction coefficient ε_i will be given by $\varepsilon_i = [\log(I_0/I)]/c_iL = d_i/c_iL$, where c_i is the concentration, L_1 the path length of solution, I_0 and I the intensities of radiation before and after absorption, and d_i the optical density. Strictly, this relationship applies to monochromatic radiation, but experience shows that in many cases it is satisfactory with the high resolving power such as has been used here, and when the intensities are related to the percentage absorption A at the peaks of a band by the relation $I_0/I = 100/(100 - A)$. Even if this relationship embodying Beer's law is not strictly valid, as discussed below, empirical calibration can be set up to give the required result (see Wright, *Ind. Eng. Chem. Anal.*, 1941, **13**, 1; Barnes, Liddel, and Williams, *ibid.*, 1943, **15**, 659). If we can assume, however, that the optical densities are additive in a mixture, we have, for a given wave-length, $d = \Sigma d_i = (c_1\varepsilon_1L + c_2\varepsilon_2L_2 + \ldots)$. For a given absorption cell, L being constant, we require to know the value of εL for each pure component at a series of key wave-lengths at each of which $d = \log 100/(100 - A)$ is measured. Equations are thus obtained from which the concentrations c_1, c_2, . . . are obtained.

In the present case of *o*-, *m*-, and *p*-cresol, at the key wave-length for any particular component, the optical densities

due to the other components can be ignored in almost all cases if suitably dilute solutions are used (Fig. 3), so that no equations have to be solved and the results can be read directly from a single graph. There is one small complication with cresols which requires consideration before the detailed analytical results are given. With *o*-cresol the band at 752 cm.$^{-1}$ remains as a single peak as the dilution is increased, but with both the *m*- and the *p*-isomer the corresponding peaks at 776 and 815 cm.$^{-1}$ split at lower concentrations into a double band with components whose relative intensity alters with changing dilution. The limiting spacing of the doublet with *p*-cresol is about 11 cm.$^{-1}$, and with *m*-cresol about 6 cm.$^{-1}$. For calibration, the stronger of the pair of peaks in each doublet has been used, since its wave-length remains almost constant. Until the exact reason for this doubling of the band with *m*- and *p*-cresol is understood, the theoretical basis for the analytical procedure is uncertain, and it is therefore to be regarded as semi-empirical. This does not, however, affect its serviceability for analysis. The doubling phenomenon is discussed below.

Figs. 3 and 4 incorporate the calibration data. It was decided to use *cyclo*hexane as solvent, since it is less offensive for general use than carbon disulphide, and is completely transparent between 12 and 14 μ. The wave-lengths of some of the absorption bands are slightly affected, not only by changes from the liquid to the solid state, but also in some cases by the particular solvent used. There is no difference between carbon disulphide and *cyclo*hexane in this respect. The absorption cell was about 0·1 mm. thick; since the same cell was used throughout, its exact thickness was not required. The absorption of solutions of *o*-cresol containing 0·5—3% by weight was measured between 700 and 850 cm.$^{-1}$ (Fig. 3). In Fig. 4 the optical density, $\log I_0/I$, is plotted as a function of concentration. With this range of dilute solutions the plot is nearly linear, suggesting that Beer's law is roughly satisfied, though this may be accidental. Similar data were

FIG. 2.



Cresols in carbon disulphide: (1) 1%; (2) 5%; (3) 20%.

obtained for *m*- and *p*-cresol. Here again, the plots are almost linear over this range of concentration. In measuring the percentage absorption, readings were taken from the smooth background of the photographic trace as base line, so that the absorption or reflection losses from the absorption cell itself are eliminated. If necessary these can be allowed for (see Nielsen and Smith, *Ind. Eng. Chem. Anal.*, 1943, **15**, 609). If the plots of Fig. 4 were strictly linear, passing through the origin, the slope $d/c = \varepsilon L$ would be a measure of the extinction coefficients. It is noteworthy that, whereas the extinction coefficients for *m*- and *p*-cresol appear to be roughly equal, that of *o*-cresol is noticeably greater, although it must again be emphasised that this difference may be in part connected with the singlet nature of the *o*-cresol band, and the exact equality of the *m*- and the *p*-derivative may be accidental.

In analysing a mixture, the spectrum of a solution in *cyclo*hexane was measured over the range 700—850 cm.$^{-1}$, and the percentage absorption at 752, 776, and 815 cm.$^{-1}$ determined. The concentration was chosen so as to give the optimum conditions for accurate measurement at the three peaks; usually, about 3 g. of sample per 100 c.c. (0·3 g. per 10 c.c.) was suitable; *e.g.*, sample *B* (Fig. 3) contained 2·93 g. per 100 c.c. The absorption percentages at the *o*-, *m*-, and *p*-peaks were 14·5, 50, and 41, which gives:

o-Cresol	0·15 g. per 100 c.c.	5% ± 0·5%
m- ,,	1·55 ,, ,,	53% ± 1%
p- ,,	1·20 ,, ,,	42% ± 1%
Total	2·90 (2·93 g. per 100 c.c. taken).	

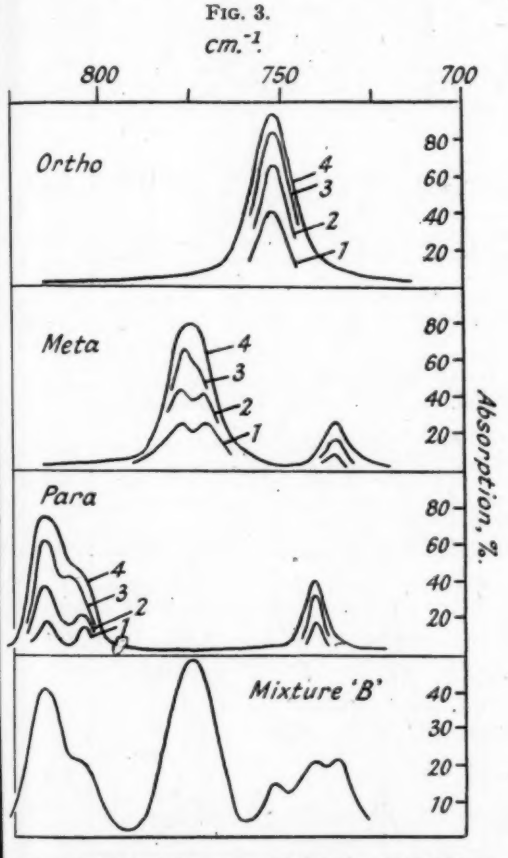
The estimated errors are based on possible errors in measuring the optical densities, and are rather greater when the optical density is very low or if it is very high. A chemical determination on this sample carried out independently in

another laboratory gave: *m*- 52·6, *o*- 5·3%. The method was tested on synthetic mixtures, and typical results are as follows:

		G. per 100 c.c.				Percentage.		
		o-.	*m*-.	*p*-.	Total.	*o*-.	*m*-.	*p*-.
M_1.	Taken	0·31	1·61	1·41	3·33	9·3	48·4	42·3
	Found	0·30	1·60	1·45	3·35	8·9	47·8	43·3
M_2.	Taken	0·60	1·61	1·27	3·48	17·2	46·2	36·6
	Found	0·60	1·65	1·30	3·55	16·9	46·4	36·7

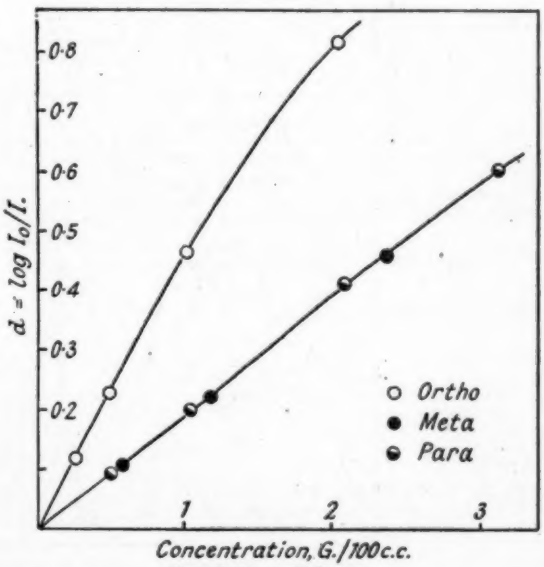
Another test sample was examined and found to contain 12, 39, and 34% respectively of *o*-, *m*-, and *p*-cresol, with 15% unaccounted for. The residue was subsequently found to consist of other components such as xylenols and phenol. The amount of material required for an analysis is very small, and the spectroscopic determination can be carried out in about ten minutes.

FIG. 3.



Cresols in cyclo*hexane*: (1) 0·5%; (2) 1·0%; (3) 2·0%; (4) 3·0%.

FIG. 4.



Cresols in cyclo*hexane*.

In Fig. 2, the spectrum of phenol is shown over the same spectral range. It is seen that small amounts of phenol in cresylic acid could be detected by means of its band at 1070 cm.$^{-1}$.

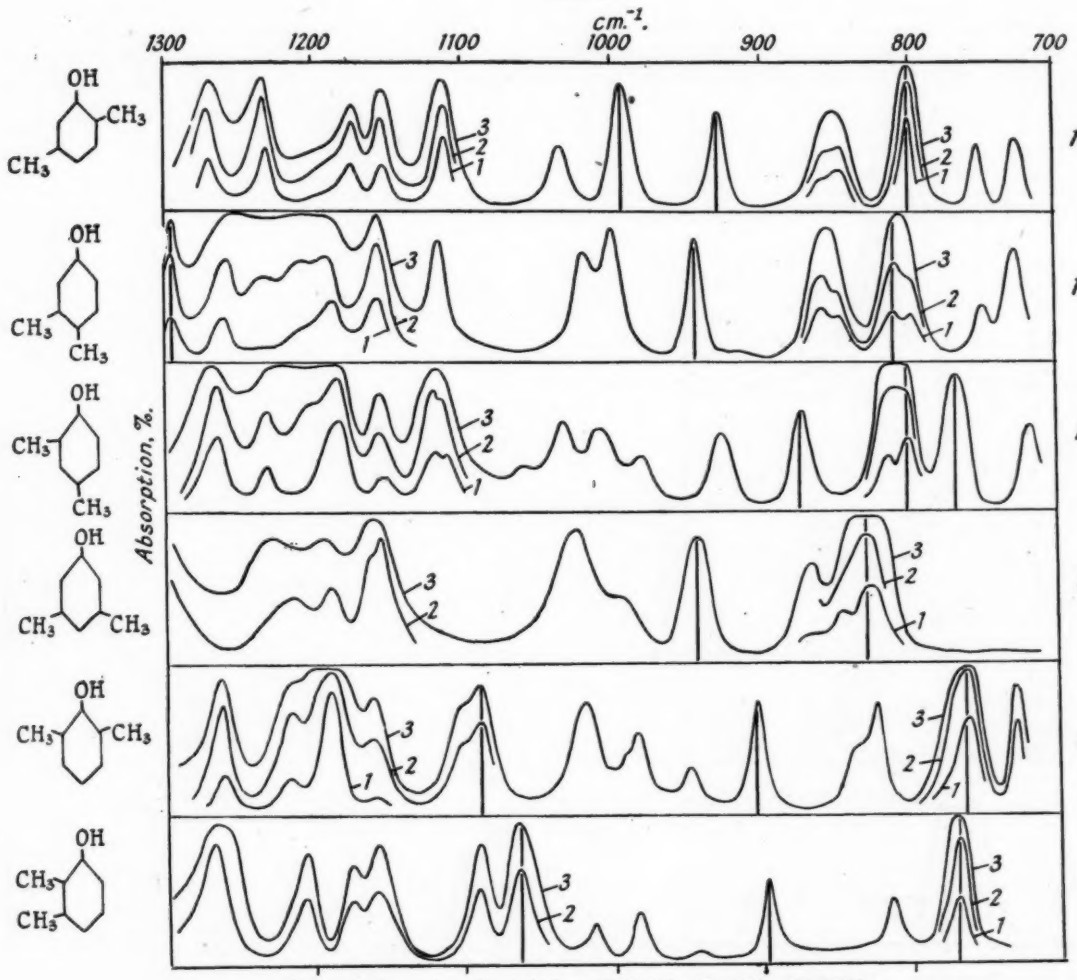
Fig. 5 shows the corresponding spectra of the six isomeric xylenols, as determined with solutions in carbon disulphide. These spectra are rather more complex than those of the cresols, but there are characteristic features, and an analysis of mixtures can be carried out in similar fashion, the accuracy obtainable being determined by the complexity of the mixture and the care taken in setting up reference calibrations. If mixtures of xylenols are first fractionated, the analysis is much simplified. For instance, 2 : 6-dimethylphenol distils off first, and if it enters a cresylic acid fraction, it can be detected by means of its bands at 1090 and 904 cm.$^{-1}$; 2 : 4- and 2 : 5-dimethylphenol next distil off together within a few degrees. Key bands for the former might be 770, 804, 873 cm.$^{-1}$, and for the latter 800, 850, and 993 cm.$^{-1}$. If 2 : 3-dimethylphenol entered this fraction, it could well be determined from the band at 1066 cm.$^{-1}$. In the top fraction 3 : 4- and 3 : 5-dimethylphenol can be measured, the former from bands at 730, 807, 855, 1116, and 1295 cm.$^{-1}$, and the latter from the band at 830 cm.$^{-1}$. Although preliminary fractionation is obviously to be avoided if possible, yet it is desirable for an initial examination, since the infra-red spectra provide indisputable evidence of the identity of the particular components present, and once this has been established an analysis may be possible without exhaustive fractionation.

It is also clear that with some suitable preliminary fractionation ethylphenols, if present, may also be identified in crude xylenol samples. In all analyses it is advantageous to use dilute solutions, unless small amounts of some particular component are being sought.

As regards the correlation of structure with vibrational spectrum, several points emerge. The most important concerns the " aromatic " band, used in particular in the analysis of cresols. As already explained, in the case of benzene

this frequency (671) has been assigned to a motion involving the oscillation of the six-carbon ring as a rigid structure through the plane of the six hydrogen atoms. With monosubstituted benzenes, regardless of the particular substituent, the frequency shifts to a value 740—760 cm.$^{-1}$, as shown in Table I. The data for the alkylbenzenes given in this and subsequent tables have been taken from a joint programme of work carried out by Dr. G. B. B. M. Sutherland and others with ourselves, and to be published shortly elsewhere.

FIG. 5.



Xylenols in carbon disulphide : (1) 1·5%; (2) 6%; (3) 17%.

TABLE I.

Phenol	751	Toluene	730	Diphenyl	752
Anisole	754	Ethylbenzene	745	Diphenylmethane	735
Aniline	753	*n*-Propylbenzene	740	*tert.*-Butylbenzene	762
N-Methylaniline	750	*iso*Propylbenzene	761	Chlorobenzene	742
NN-Dimethylaniline	749	Diphenylamine	747	Bromobenzene	740
NN-Diethylaniline	748				

With disubstituted benzenes (Table II) the corresponding vibration frequency moves steadily towards higher frequencies in passing along the series *o-*, *m-*, *p*, independently of the nature of the substituent groups. With each class of isomer, the frequency remains within fairly close limits, but measurements are needed with other compounds before rules can be set up to express how the small variations are connected with the particular nature of the substituent groups, or with steric effects.

TABLE II.

	o-.	*m-*.	*p-*.		*o-*.	*m-*.	*p-*.
Xylenes	743	765	790	*NN*-Dimethyltoluidines	—	—	806
Ethyltoluene	752	782	826	*NN*-Diethyltoluidines	—	—	813
Diethylbenzenes	—	792	828	*N*-Methyltoluidines	—	—	810
Toluidines	753	774	810	Di*iso*propylbenzenes	—	793	827
Cresols	752	775	827	Di-*tert.*-butylbenzenes	—	—	829
Dichlorobenzenes	750	—	818				

The corresponding intense absorption band appears with the xylenols, and the exact value of the frequency depends on the arrangement of the substituent groups; *e.g.*, all those having a 1 : 2 : 4-grouping, *viz.*, 1 : 2 : 5-, 1 : 3 : 4-, and 1 : 2 : 4-xylenol, have the band at 800—810 cm.$^{-1}$; those with the 1 : 2 : 3-grouping, *viz.*, 1 : 2 : 3- and 1 : 2 : 6-xylenol, have the band at 760—770 cm.$^{-1}$, and that with a 1 : 3 : 5-grouping at 833 cm.$^{-1}$. As with the disubstituted benzenes, it seems that the frequency rises in value as the substituent groups are spread around the aromatic nucleus, and is smallest when these groups are in closest proximity. Moreover, the value of this particular vibration frequency of trisubstituted benzenes seems to be to a large extent independent of the nature of the substituent groups. Table III gives results for xylenols, xylidines, and trimethylbenzenes.

TABLE III.

Type 1 : 2 : 3.				Type 1 : 2 : 4.				Type 1 : 3 : 5.			
(1).	(2).	(3).	cm.$^{-1}$.	(1).	(2).	(4).	cm.$^{-1}$.	(1).	(3).	(5).	cm.$^{-1}$.
CH_3	CH_3	CH_3	766	OH	CH_3	CH_3	804	CH_3	CH_3	CH_3	834
CH_3	CH_3	OH	770	CH_3	CH_3	CH_3	806	CH_3	CH_3	OH	830
CH_3	OH	CH_3	761	CH_3	OH	CH_3	800	CH_3	CH_3	NH_2	828
CH_3	NH_4	CH_3	761	CH_3	CH_3	OH	807				
				CH_3	NH_2	CH_3	797				
				CH_3	CH_3	NH_2	810				
				NH_2	CH_3	CH_3	813				

Apart from these structural correlations, the other interesting feature of the " aromatic " band is the doubling shown with some compounds at lower concentrations. As stated already, *o*-cresol shows no splitting, but *m*- and *p*-cresol do. In order to find possible causes for this effect, we have measured the spectra of a large number of mono- and di-substituted benzenes in dilute solution over the relevant range of wave-lengths. None of the monsubstituted derivatives listed in Table I shows a double band, nor any of the disubstituted derivatives of Table II, with the possible exception of *o*-dichlorobenzene. In the latter case, however, the spectrum suggests that there are two bands which accidentally fall close together, and it seems improbable that the effect is due to the same cause as with *m*- and *p*-cresol. As regards the xylenols, there is no splitting of the bands of the 1 : 2 : 6- or the 1 : 2 : 5-isomer at 761 and 800 cm.$^{-1}$, respectively, but doubling occurs with each of the other isomers.

The most natural hypothesis is to assume that the doubling phenomenon results from association through hydroxyl groups, although the exact mechanism is not clear. It might be possible to explain the absence of doubling in some cases by diminished association due to steric hindrance caused by methyl groups protecting the hydroxyl group. Further, there are peculiar variations of the absorption bands with concentration in the region 1100—1300 cm.$^{-1}$ with many of the hydroxylic compounds, particularly those showing a doubling of the " aromatic " band. This effect can well be seen by comparing the spectra of a solution of phenol in carbon disulphide with that of liquid phenol (Barnes, Liddel, and Williams, *loc. cit.*), and the variations are not merely due to slight displacement of bands by change of solvent or state of aggregation. These variations are almost certainly connected with the effect of varying association on the deformational frequency of the O–H bond. On the other hand, these explanations are not very satisfactory, for the phenol band at 751 cm.$^{-1}$ is single, and until further data on this phenomenon are available, further discussion must be postponed.

We are grateful to the Department of Scientific and Industrial Research and to the Government Grant Committee of the Royal Society for financial support.

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69. *The Resolution of Propenylethynylcarbinol.*

By J. KENYON and R. POPLETT.

By fractional crystallisation of the cinchonidine salt of its hydrogen phthalic ester, *dl*-propenylethynylcarbinol has been separated into its *d*- and *l*-forms: the (+)carbinol on reduction yielded (−)ethyl-*n*-propylcarbinol.

IN view of its high degree of unsaturation, it was considered of interest to attempt the preparation of optically active propenylethynylcarbinol and ascertain whether its rotatory powers and optical rotatory dispersion showed any marked anomalies. Furthermore, since this alcohol undergoes anionic rearrangement in the presence of acid (Jones and McCombie, J., 1943, 261, and subsequent papers), it was likely that the optically active material would prove useful in the study of the kinetics of anionotropic rearrangements (this has now proved to be the case; see Braude and Jones, J., 1944, 436). *dl*-Propenylethynylcarbinol was prepared and investigated by Jones and McCombie (J., 1942, 734), and that used in the present work was very generously placed at our disposal by Dr. E. R. H. Jones.

It is interesting to compare the specific rotatory powers, $[\alpha]_{5893}^{20°}$, of the following four closely related alcohols:

$CHMe{:}CH{\cdot}CH(OH){\cdot}C{:}CH$	70·6°	$CH_3Me{\cdot}CH_2{\cdot}CH(OH){\cdot}CH_2{\cdot}CH_3$	7·1°
$CHMe{:}CH{\cdot}CH(OH){\cdot}CH_2{\cdot}CH_3$	13·1	$CH_2Me{\cdot}CH_2{\cdot}CH(OH){\cdot}CH{:}CH_2$	28·9 *

* Kenyon and Snellgrove (J., 1925, 127, 1178).

EXPERIMENTAL.

dl-*Propenylethynylcarbinyl Hydrogen Phthalate.*—A mixture of the carbinol (20 g.), phthalic anhydride (30·8 g.), and pyridine (17 g.) was kept at 55—60° for 1 hour and then at room temperature for 2 days. The resulting viscous liquid was diluted with an equal volume of acetone and decomposed with a slight excess of cold dilute hydrochloric acid; the precipitated pasty solid rapidly hardened, and after several hours the resulting crystalline *ester* was collected

and dried (48 g., yield 94%), m. p. 85—86°. It separated from ether–light petroleum as hard, transparent prisms, m. p. 86—87° (Found, on titration with 0·1N-NaOH: *M*, 244. $C_{14}H_{12}O_4$ requires *M*, 244).

(+)*Propenylethynylcarbinyl Hydrogen Phthalate.*—A solution of the *dl*-ester (77 g.) and cinchonidine (92·4 g.) in ethyl acetate (400 c.c.), after standing overnight, deposited a mixture of the cinchonidine salts of the dextrorotatory and the lævorotatory hydrogen phthalate (the former in excess). From this mixture, after four extractions with boiling ethyl acetate, the cinchonidine salt of (+)propenylethynylcarbinyl hydrogen phthalate (25 g.) remained as a residue of minute, round crystals, m. p. 155—156° (decomp.). This salt, mixed with acetone, was decomposed with cold dilute hydrochloric acid, and the resulting (+)*propenylethynylcarbinyl hydrogen phthalate* precipitated by the addition of water. It separated from carbon disulphide in hard, irregular crystals, m. p. 56—57° (Found, on titration with 0·1N-NaOH: *M*, 244). Rotatory powers are given in the table below.

(+)*Propenylethynylcarbinol.*—This (+)hydrogen phthalate (24 g.) was heated with 5N-sodium hydroxide (2·5 mols.) on the steam-bath for 10 minutes, and the resulting cooled solution extracted with ether. The ethereal layer was separated, washed with water, dried, and evaporated, and the residue (7·3 g.) distilled. The (+)propenylethynylcarbinol thus obtained had b. p. 157—159°, $n_D^{16\cdot5°}$ 1·4645, $d_4^{14°}$ 0·9125, $d_4^{20°}$ 0·9090, $d_4^{30°}$ 0·9030, $d_4^{40°}$ 0·8970. Rotatory powers are given in the table.

(−)*Propenylethynylcarbinyl Hydrogen Phthalate.*—The mixed filtrates from the first two extractions of the cinchonidine salt of the dextrorotatory hydrogen phthalate were evaporated, and the residue mixed with a little acetone and decomposed with a slight excess of dilute hydrochloric acid. The resulting acid phthalic ester had $[\alpha]_{5893}$ − 24° in ethyl-alcoholic solution. By fractional crystallisation from carbon disulphide, which rapidly separated the less soluble racemic form, the almost optically pure (−)*hydrogen phthalate* was obtained as minute, round crystals, m. p. 62—64°; $[\alpha]_{5893}$ − 41·1° (*c*, 1; *l*, 2) in ethyl-alcoholic solution (Found, by titration: *M*, 245).

Specific rotatory powers of (+)*propenylethynylcarbinyl hydrogen phthalate* (*l*, 2).

Solvent.	*c*, g. per 100 c.c. soln.	Temp.	$[\alpha]_{6438}$.	$[\alpha]_{5893}$.	$[\alpha]_{5780}$.	$[\alpha]_{5461}$.	$[\alpha]_{4358}$.
EtOH	1·568	16°	+38·6°	+47·5°	+47·2°	+60·5°	+110·8°
CS_2	1·024	18	21·6	26·5	27·3	33·1	60·9
$CHCl_3$	1·662	20	21·2	22·0	22·4	26·3	47·5
C_6H_6	2·750	17	12·3	15·1	15·4	17·8	36·0

Observed rotatory powers of (+)propenylethynylcarbinol (*l*, 0·25; *t*, 19·5°):

λ	6438	5893	5780	5461	4358
α_λ	+13·05°	+16·06°	+16·59°	+19·15°	+34·95°

Reduction of (+)*Propenylethynylcarbinol to* (−)*Ethyl-n-propylcarbinol.*—This reduction was kindly carried out for us by Dr. E. R. H. Jones, using palladium–norit catalyst (J., 1942, 734). The resulting saturated carbinol had b. p. 133—134°, $n_D^{20°}$ 1·4140, $\alpha_{5893}^{18°}$ − 1·46° (*l*, 0·25), whence $[\alpha]_{5893}^{18°}$ − 7·13° (Pickard and Kenyon, J., 1913, **103**, 1935) give $n_D^{20°}$ 1·4141).

Ethyl-*n*-propylcarbinol has never been obtained optically pure by the fractional crystallisation of alkaloidal salts of its hydrogen phthalate, but (+)ethyl-*n*-propylcarbinol obtained by the catalytic reduction of (+)-γ-methyl-α-ethylallyl alcohol had $[\alpha]_{5893}^{20°}$ + 7·09° (Airs, Balfe, and Kenyon, J., 1942, 19); it appears very probable, therefore, that these three alcohols—the saturated, the ethylenic, and the acetylenic—are optically pure.

Thanks are expressed to the Government Grants Committee of the Royal Society and to Imperial Chemical Industries Ltd. for grants.

BATTERSEA POLYTECHNIC, LONDON, S.W.11. [*Received, November 21st*, 1944.]

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70. *The Reactions of Grignard Reagents with Some Zinc Chloride Double Salts of Diazonium Compounds.*

By HERBERT H. HODGSON and EWART MARSDEN.

The complex decompositions which occur when Grignard reagents from bromo- and iodo-compounds are treated in dry ether with zinc chloride double salts of diazotised amines, $(ArN_2^{++})_2\bar{Z}n\bar{C}l_4^-$, include (*a*) the formation of aryl halides but not aryl chlorides; (*b*) the production of mixed azo-compounds, *e.g.*, methyl-, ethyl-, or phenyl-azo-benzenes and -naphthalenes, (*c*) the formation of αα′- and ββ′-azonaphthalenes from the double salts with diazotised α- and β-naphthylamines. In no cases were alkyl-benzenes or -naphthalenes or phenylnaphthalenes observed.

No study is on record of the reactions of Grignard reagents with aromatic diazo-compounds, and since such reactions must of necessity be carried out in anhydrous media, the double salts of zinc chloride with diazonium compounds were selected for the purpose; these salts can be adequately dried and are stable for considerable periods of time. It was first established that neither metallic magnesium nor methyl iodide, ethyl bromide or iodide, or phenyl bromide reacted with the diazo-double salts, so the vigorous reactions occurring when these salts were added to the solutions of the Grignard compounds in dry ether could only be due to the latter compounds as such. After the reactions were completed, the mixtures were steam-distilled; they were not previously acidified owing to the danger of decomposing any azo-compound that might have been formed and also in order to avoid any conversion of an alkyl azo-compound into the isomeric hydrazine (cf. Wieland, "Die Hydrazine," Stuttgart, 1913, pp. 130 *et seq.*).

From a consideration of both the steam-volatile and the non-volatile products, it was obvious that several simultaneous reactions had taken place.

(*a*) The production of volatile bromo- and iodo-compounds (a chloro-compound was never detected) indicates that the Grignard reagent must have reacted in similar fashion to the anionoid halogen in the Sandmeyer reaction (cf. Hodgson and Birtwell, J., 1941, 770). Iodination by the Grignard reagent, which, in the dry ether employed, could only have occurred *via* anionoid iodine, since ionisation of the Grignard reagent is excluded, supports the earlier observation by Hodgson and Birtwell (*loc. cit.*) that potassium iodide will not react with a diazo-compound in acid solution in presence of a reducing agent, and consequently indicates that iodination occurs *via* the anionoid iodine in the anion I_3'.

(*b*) From the formation of mixed azo-compounds, the anionoid alkyl or aryl group of the Grignard reagent must have become attached at the nitrogen atom more remote from the carbon atom to which the diazo-group is attached. When the double salts of zinc chloride with diazotised aniline and *p*-toluidine reacted with methyl- and ethyl-magnesium halides, no azobenzene or azotoluene was detected, so the azobenzene and *p*-benzeneazotoluene obtained with phenylmagnesium bromide must have resulted from the reaction of its phenyl group.

(*c*) After reaction, however, of the Grignard reagents with the double salts of zinc chloride and diazotised α- and β-naphthylamine, the radicals left after the liberation of nitrogen either combine with each other to form dinaphthyls, as with the double salts from diazotised aniline and *p*-toluidine, which afford some diaryl, or they react with undecomposed diazo-salt to form αα′- and ββ′-azonaphthalene, a reaction not given by the aniline and *p*-toluidine double salts. The yield of azo-compounds, however, is almost negligible when the decompositions are carried out with methyl- and ethyl-magnesium halides, but reaches 20% when phenylmagnesium bromide is used. It would appear, therefore, that the naphthyl radicals are more prone than the aryl radicals to unite with themselves; in no case, however, could phenylnaphthalene be detected, the phenyl radical thus resembling the methyl and the ethyl radical in not forming methyl- and ethyl-benzenes or -naphthalenes in the Grignard decompositions.

Experimental.

Preparation of the Zinc Chloride Double Compounds of Aryl- or Naphthyl-diazonium Chlorides.—The amine (0·1 g.-mol.) is dissolved in hydrochloric acid (24 c.c., *d* 1·18) and water (24 c.c.) (with heating if necessary), diazotised at 0° with sodium nitrite (7 g.) dissolved in water (24 c.c.), and filtered. (If ice is added, the total volume should not exceed 150 c.c.) Solid zinc chloride (7 g.) is now added, and the resulting double chloride is filtered off, washed with a few drops of water, and dried first on filter-paper by suction and then in a desiccator for several days.

Reaction of Grignard Reagents with Zinc Chloride Double Salts: General Procedure.—The Grignard reagent was prepared in one equivalent excess by reaction of the alkyl or aryl halide in excess with magnesium (0·5 g.) in dry ether (50 c.c.), a crystal of iodine being added as catalyst. Reagents designated A, B, C, and D respectively were thus obtained from methyl iodide, ethyl bromide and iodide, and phenyl bromide, and these were treated with the dry finely powdered benzene- or naphthalene-diazonium chloride double salt with zinc chloride (0·01 g.-mol.). After the violent evolution of nitrogen had abated, the mixtures were refluxed for a further 15 minutes and then steam-distilled. The steam-distillate contained aryl or naphthyl bromide or iodide, but no chloro-compound, and also, when bromobenzene was used, diphenyl, the corresponding dialkyl from the aliphatic halides having been evolved as a gas. In addition, some azo-products were also steam-volatile, but otherwise they were identified in the steam-flask residues.

Data from Individual Reactions.—In all cases the name of the parent amine stands for the double salt $(\overset{++}{ArN_2})_3\overset{--}{ZnCl_4}$.

Aniline. With A, the whole of the reaction product was volatile in steam and contained iodobenzene, diphenyl, and methylazobenzene (*ca.* 15%), which was detected by reduction and diazotisation of the steam distillate (see under B); neither toluene nor azobenzene was detected.

With B, the products were diphenyl, bromobenzene, and ethylazobenzene; the last was estimated by reduction of the steam-volatile liquid with zinc dust and hydrochloric acid, whereupon, after filtration, 3 c.c. of N-sodium nitrite were absorbed, corresponding to the formation of 15% of ethylazobenzene from the double salt; no azobenzene was observed.

With C, the products were as with B, but iodobenzene was formed in greater amount than bromobenzene in B.

With D, the steam-distillate contained diphenyl and azobenzene; on reduction as for B, the latter required 4·2 c.c. of N-sodium nitrite, corresponding to 21% conversion of the double salt.

p-Toluidine. Reagent A afforded a large yield of *p*-iodotoluene, together with *pp*′-ditolyl and a little methylazotoluene, detected by reduction and diazotisation as above. B and C gave a little ethylazotoluene, but the yield of *p*-iodotoluene from C exceeded that of bromobenzene from B. With D, *p*-bromotoluene and *p*-benzeneazotoluene came over with the steam, the latter compound (identified by m. p. and mixed m. p. with an authentic specimen) in 21% yield.

α-Naphthylamine. With A, the steam-volatile compounds were naphthalene, α-iodonaphthalene, and α-methylazonaphthalene; the azo-compound was found in 7% yield but could not be isolated owing to its admixture with much greater amounts of the other substances and to its great solubility in all solvents tried. The non-volatile matter was αα′-dinaphthyl (*ca.* 1 g.), identified by m. p. and mixed m. p. with an authentic specimen. Azonaphthalene could not be detected in the non-volatile product, which gave no colour with concentrated sulphuric acid, and when treated with hydrochloric acid and zinc dust afforded no α-naphthylamine. With B, the steam-volatile product contained α-bromonaphthalene and *α-ethylazonaphthalene* (5% yield); the latter crystallised from the steam-distillate in yellow prisms, m. p. 25—27° (Found: N, 15·3. $C_{12}H_{12}N_2$ requires N, 15·2%), which were very soluble in light petroleum and dissolved in concentrated sulphuric acid to give a yellow solution. The amount of azonaphthalene in the non-volatile product was negligible, and the yield of αα′-dinaphthyl 0·7 g. With D, the steam-distillate contained only diphenyl and α-bromonaphthalene; the non-volatile matter (*ca.* 2·0 g.) was reduced in the steam flask with zinc and hydrochloric acid, and the mixture made alkaline with sodium hydroxide and steam-distilled; aniline passed over, and titration with N-sodium nitrite (0·6 c.c.) indicated the formation of 6% of α-phenylazonaphthalene. The flask liquor, when acidified and titrated, required 5·15 c.c. of N-sodium nitrite, corresponding to the formation of 22·75% of αα′-azonaphthalene from the double salt. A separate experiment, in which the non-volatile residue was reduced, afforded 0·6 g. of αα′-dinaphthyl (m. p. and mixed m. p.) by extraction from the insoluble matter with boiling ethyl alcohol.

β-Naphthylamine. With A, the steam-volatile products included naphthalene, β-iodonaphthalene, and β-methylazonaphthalene. The last solidified in yellow crystals (in about 5% yield) but could not be separated from its companions. The non-volatile product (*ca.* 1 g.) was ββ′-dinaphthyl, only a trace of ββ′-azonaphthalene being formed. With B, the steam-volatile product included naphthalene, β-bromonaphthalene, and *β-ethylazonaphthalene* (10% yield). The last crystallised from the distillate in yellow prisms, m. p. 65—68° (depressed by naphthalene) (Found: N, 15·4. $C_{12}H_{12}N_2$ requires N, 15·2%). The non-volatile matter was treated as for that from α-naphthylamine and afforded 2·5% of ββ′-azonaphthalene, with ββ′-dinaphthyl (0·8 g.) as the main constituent. With D, the steam-volatile products were diphenyl, naphthalene, and β-bromonaphthalene; the non-volatile residue (2·2 g.), treated as for that from α-naphthylamine, was a mixture of ββ′-dinaphthyl, ββ′-azonaphthalene (20%), and β-phenylazonaphthalene (7%).

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TECHNICAL COLLEGE, HUDDERSFIELD. [*Received, November 27th,* 1944.]

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71. *A New Method for the Preparation of* p-*Dialkylaminobenzaldehydes.*

By JAMES C. DUFF.

After dimethylaniline, hexamethylenetetramine, acetic and formic acids have been heated together, *p*-dimethylaminobenzaldehyde can be separated in satisfactory yield by adding the mixture to dilute hydrochloric acid. The corresponding derivatives from other dialkyl- and from benzylalkyl-anilines have also been prepared by this method.

p-DIALKYLAMINOBENZALDEHYDES have already been prepared by the following methods: (1) Ullmann and Frey (*Ber.*, **1904**, **37**, 855) used a reaction between a dialkylaniline, *p*-nitrosodimethylaniline, and formaldehyde. This method has been developed and recommended for preparing *p*-dimethylaminobenzaldehyde (*Org. Synth.*, Coll. Vol. 1, 1932, 208). (2) D.R.-P. 105,105 describes the preparation of *p*-dimethyl- and *p*-diethyl-aminobenzaldehydes from interaction of the dialkylaniline, formaldehyde, and *m*-nitrobenzenesulphonic acid in the presence of iron and hydrochloric acid. (3) D.R.-P. 118,567 describes a modification of method (2), using an amino-sulphonic acid instead of the corresponding nitro-acid. (4) In D.R.-P. 103,578 use is made of a reaction between a dialkylaniline, formaldehyde, and a hydroxylaminotoluenesulphonic acid. (5) Vilsmeier and Haack (*Ber.*, 1927, **60**, 119) used a reaction between *N*-formylmethylaniline, phosphorus oxychloride, and a dialkylaniline, obtaining very good yields of *p*-aldehydes from dimethyl-, diethyl-, and benzylmethyl-aniline.

For methods (2), (3), and (4) yields are not recorded. Dippy, Hogarth, Watson, and Williams (*J. Soc. Chem. Ind.*, 1937, **56**, 346T) investigated the first three methods and concluded that (1) was satisfactory, (2) unsatisfactory, and (3) had to be modified to give good yields of *p*-dimethyl- and *p*-diethyl-aminobenzaldehydes. Methods (4) and (5) are the only recorded methods for preparing *p*-benzylalkylaminobenzaldehydes.

The author (J., 1941, 547) has already described a method for the preparation of *o*-hydroxy-aldehydes from the reaction between phenols and hexamethylenetetramine in glyceroboric acid. It was decided then to investigate the possibility of introducing an aldehyde group into dialkylanilines by a similar method. Glyceroboric acid was found unsuitable as an acid medium for the reaction, but acetic acid, which was not a success with phenols, was found to be suitable for use with the tertiary amines, especially when formic acid also was present.

Formic acid alone gave only poor yields of the aldehydes; acetic acid alone gave satisfactory yields, but the aldehydes were slightly discoloured. After several hours' heating of the dialkylaniline and hexamethylenetetramine in a mixture of acetic and formic acids the resulting solution was poured into 0·5N-hydrochloric acid, and the aldehyde separated in almost pure condition. The yields compare favourably with those recorded for other general methods. This new method has been applied successfully to dimethyl-, diethyl-, and methylethyl-aniline, and to dimethyl-*m*-toluidine, but failed, as expected, with dimethyl-*o*- and -*p*-toluidines. A modified procedure was necessary for the purification of the *p*-aldehydes obtained from benzylmethyl- and benzylethyl-anilines. The mechanism of the reaction could not be established by the separation of any intermediate compound. It probably proceeds in the same way as that suggested for the formation of phenolic aldehydes (*loc. cit.*) and may therefore be as follows:

$$3NR_2\cdot C_6H_5 + C_6H_{12}N_4 \longrightarrow NH_3 + 3NR_2\cdot C_6H_4\cdot CH_2\cdot N{:}CH_2$$

followed by isomerisation and hydrolysis:

$$NR_2\cdot C_6H_4\cdot CH_2\cdot N{:}CH_2 \longrightarrow NR_2\cdot C_6H_4\cdot CH{:}N\cdot CH_3 \xrightarrow{H_2O} NR_2\cdot C_6H_4\cdot CHO + CH_3\cdot NH_2$$

The dilute hydrochloric acid used in the separation of the aldehyde hastened the hydrolysis and served to retain in solution the more basic by-products.

EXPERIMENTAL.

Preliminary experiments showed that a mixture of glacial acetic acid and 90% formic acid was more effective than when either acid was used alone. Anhydrous formic acid was less useful than the 90% acid in the mixture. This mixed acid had to be added in portions during the reaction, apparently because the formic acid had a reducing effect, indicated by the evolution of carbon dioxide. Alcohol was used in the process merely to assist in bringing more of the hexamethylenetetramine into solution initially.

All the aldehydes now prepared have been made by other methods, and, except *p*-methylethylaminobenzaldehyde, they agree with the recorded descriptions of their properties. They all give bright yellow condensation products with aniline, reduce Tollens's reagent, and form phenylhydrazones and/or *p*-nitrophenylhydrazones.

Method of Preparation for p-Dialkylaminobenzaldehydes.—To the dialkylaniline (30 g.), hexamethylenetetramine (40 g.), and 95% ethyl alcohol (20 ml.), heated under reflux on a boiling water-bath, 30 ml. of a mixture of glacial acetic acid (45 ml.) and 90% formic acid (45 ml.) were added, and the remainder of the mixed acid was added in 10-ml. portions at 30-min. intervals. After a total of 5 hours' heating, the hot liquid mixture was poured with stirring into 600 ml. of approx. 0·5N-hydrochloric acid and left for several hours. The aldehyde separating was purified either by crystallisation from 30% alcohol or by distillation under reduced pressure. In the case of *p*-dimethylaminobenzaldehyde the acid filtrate obtained after removal of the aldehyde was examined for by-products by adding excess of sodium hydroxide solution. This produced about 20 g. of yellow oil, from which about 3 g. of bis-(*p*-dimethylaminophenyl)methane crystallised. Distillation of the remaining oil produced a further 4 g. of *p*-dimethylaminobenzaldehyde, distilling at 145°/10 mm. The remainder of the oil was not identified and could not be distilled. *p*-Dimethylaminobenzaldehyde (yield 14 g.) was obtained in colourless leaflets, m. p. and mixed m. p. 73°, b. p. 180°/20 mm. A phenylhydrazone, m. p. 148°, and an oxime, m. p. 144° (Found : N, 17·3. Calc. for $C_9H_{12}ON_2$: N, 17·1%), were prepared by the usual methods.

p-Diethylaminobenzaldehyde was purified by crystallisation from 30% alcohol, yield 14 g., m. p. 41°. The oxime had m. p. 93°, and the phenylhydrazone m. p. 121° (Found : N, 15·9. Calc. for $C_{17}H_{21}N_3$: N, 15·7%); Ullmann and Frey (*loc. cit.*) give m. p. 93° and 103°, respectively.

p-Methylethylaminobenzaldehyde separated as an oil. It distilled at 180—185°/20 mm. and solidified (12 g.); m. p. 44° (Found : N, 8·7. Calc. for $C_{10}H_{13}ON$: N, 8·6%). Ullmann and Frey (*loc. cit.*) record m. p. 14°. They found N, 9·14% and do not record the yield. The phenylhydrazone had m. p. 114°, in agreement with Ullmann and Frey.

4-Dimethylamino-2-methylbenzaldehyde from *N*-dimethyl-*m*-toluidine was purified by crystallisation from 30% alcohol; yield 6 g., m. p. 67° (Found : N, 8·8. Calc. for $C_{10}H_{13}ON$: N, 8·6%). Dimethyl-*o*- and -*p*-toluidines did not yield an aldehyde, being recovered unchanged in each case.

For the preparation of *p*-benzylmethylaminobenzaldehyde the process was modified as follows : To benzylmethylaniline (40 g.), hexamethylenetetramine (40 g.), and ethyl alcohol (25 ml.), heated under reflux on a boiling water-bath, were added 30 ml. of a mixture of glacial acetic acid (75 ml.) and 90% formic acid (25 ml.), the remainder being added in 15-ml. portions at 40-min. intervals. After heating and treatment as in the general method (above), the separated oil was taken up in ether (150 ml.) and shaken with sodium bisulphite solution. The crystalline addition compound was collected, dissolved in hot 2N-hydrochloric acid, and the aldehyde precipitated by excess of sodium hydroxide solution; yield 20 g., m. p. 63° (Found : N, 6·3. Calc. for $C_{15}H_{15}ON$: N, 6·2%). The p-*nitrophenylhydrazone*, m. p. 179°, was obtained as dark red leaflets (Found : N, 15·7. $C_{21}H_{19}O_3N_4$ requires N, 15·5%).

By the same process benzylethylaniline (40 g.) yielded *p*-benzylethylaminobenzaldehyde, but no addition compound with sodium bisulphite could be formed. The aldehyde was purified by extraction of the dried oil with light petroleum (b. p. 60—80°) to remove unchanged amine, 16 g. being left as a thick yellow oil which set to a glassy mass at 0° (in agreement with D.R.-P. 103,578). The p-*nitrophenylhydrazone*, m. p. 164°, was obtained in dark red leaflets (Found : N, 15·2. $C_{22}H_{22}O_2N_4$ requires N, 15·0%).

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THE TECHNICAL COLLEGE, BIRMINGHAM. [*Received, December 8th*, 1944.]

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72. *Synthetical and Stereochemical Investigations of Reduced Cyclic Bases. Part I. Hydrogenation Products of Indole and the Exhaustive Methylation of an* N-*Methyloctahydroindole.*

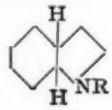
By F. E. KING, J. A. BARLTROP, and R. J. WALLEY.

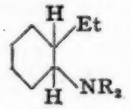
Raney nickel reduction of indole in methanol solution gives N-*methyloctahydroindole* (I, R = Me), probably the *cis*-isomer. Unlike *cis*-2-methyloctahydroindole, which affords a dimethyl-2-*n*-propyl*cyclo*hexylamine (Fujise, *Sci. Papers Inst. Phys. Chem. Res. Tokyo*, 1928, **9**, 91), exhaustive methylation of the base (I, R = Me) unexpectedly severs the nitrogen atom from the *cyclo*hexane ring with the formation of *dimethyl-β-cyclohexylethylamine*, which was synthesised for comparison. In order to determine the configuration of " perhydroindole " (Willstätter, Seitz, and v. Braun, *Ber.*, 1925, **58**, 385), cis- and trans-2-*ethyl*cyclo*hexylamine* (II, R = H) have been synthesised and appear to demonstrate the identity of this base with the *cis*-isomeride.

THE preparation of *cis-trans*-forms of decalin, hydrindane, and bi*cyclo*octane, chiefly by Hückel and Linstead, and the physical and chemical properties of the isomerides, have very largely confirmed the predictions of the tetrahedral theory of stereochemistry in its application to *ortho*-carbodicyclic systems. The existence of stereoisomerides has also been recorded when the dicyclic nucleus includes a hetero-atom, as in decahydroquinoline (Hückel and Stepf, *Annalen*, 1927, **453**, 163) and decahydro*iso*quinoline (Helfer, *Helv. Chim. Acta*, 1923, **6**, 785; 1926, **9**, 814), but a review of the literature reveals that less is known of other types of condensed heterocyclic structures, and in the octahydroindole series, for example, *cis-trans*-isomerism has apparently never been observed.

The absence of stereoisomerism among the octahydroindoles is not likely to be due, *a priori*, to the excessive instability of one of the two theoretically possible structures on account of valency distortion. The normal angle of the carbon–nitrogen–carbon valencies is known to be virtually identical with that of the carbon bonds in the unstrained *cyclo*pentane ring, so the stereochemistry of octahydroindole may be likened to that of hydrindane. Accordingly, on this analogy it is to be expected that the *cis*-structure would be strainless and readily formed, and that the *trans*-form, while theoretically capable of synthesis from the appropriate monocyclic intermediates, would, on account of its strained configuration, be produced in relatively small amounts during the complete hydrogenation of indole.

The reduction of indole to an octahydro-derivative has been carried out by Willstätter and Jacquet (*Ber.*, 1918, **51**, 777) at room temperature in acetic acid over platinum, and by Adkins and Coonradt (*J. Amer. Chem. Soc.*, 1941, **63**, 1563) at high temperature and pressure with a Raney nickel catalyst. The m. p.'s of the derived benzenesulphonamides indicate that despite these widely different conditions the reduction products were essentially identical. According to the tetrahedral theory this hydroindole is probably the *cis*-isomer, but its exact structure has never been ascertained. On the other hand, the octahydro-derivative obtained by the platinum-catalysed reduction of 2-methylindole in acetic acid has definitely been shown to possess the *cis*-configuration by applying the process of exhaustive methylation (Fujise, *loc. cit.*). Hydrogenation of the resulting methine gave a dimethyl-2-*n*-propyl*cyclo*hexylamine, at once recognised as the *cis*-isomeride since it had previously been derived from that decahydroquinoline already known from the work of Hückel and Stepf (*loc. cit.*) to possess the *cis*-configuration. In view of its formation under identical conditions, it is evident that the known octahydroindole (I, R = H) is also a *cis*-compound, but in order to obtain conclusive evidence on this point, we proposed to submit the base to exhaustive methylation and to compare the degradation product with the appropriate synthetical *cis-trans*-isomers of definitely established constitution.

(I.) 



(II.)

By analogy with the 2-methyl derivative, the exhaustive methylation of octahydroindole was expected to lead to a vinylamine and on subsequent reduction to yield one of the stereoisomeric N-*dimethyl*-2-*ethyl*-cyclo*hexylamines* (II, R = Me). These compounds have not hitherto been described, but in the course of experiments on the nickel-catalysed reduction of indoles, v. Braun, Bayer, and Blessing (*Ber.*, 1924, **57**, 392) isolated a " perhydroindole," which was eventually formulated as 2-ethyl*cyclo*hexylamine (II, R = H) (Willstätter, Seitz, and v. Braun, *loc. cit.*). No opinion has been expressed as to its stereochemical structure, and syntheses of the *cis-trans*-isomerides of ethyl*cyclo*hexylamine were therefore undertaken, both to provide intermediates for the preparation of the isomeric tertiary amines (II, R = Me) and to throw light on the constitution of perhydroindole.

The synthetical work originated from 2-ethyl*cyclo*hexanone (Vavon and Mitchovitch, *Bull. Soc. chim.*, 1929, **45**, 961), prepared by acid hydrolysis of ethyl 2-ethyl*cyclo*hexanonecarboxylate. The ketone afforded a 2 : 4-*dinitrophenylhydrazone*, and reduction of the ketoxime under suitable conditions gave the desired isomeric ethyl*cyclo*hexylamines. The configurations assigned to the products are based on Skita's observation (*Ber.*, 1920, **53**, 1792) that reduction in acid media leads predominantly to the formation of *cis*-, whereas reduction in neutral or alkaline conditions affords the *trans*-isomerides. As certain physical properties, *e.g.*, b. p., density, and refractive index, are generally slightly higher for the *cis*- than for the *trans*-forms (Auwers, *Annalen*, 1919, **419**, 92; 1920, **420**, 84), the validity of Skita's generalisation is readily established, and this has already been done with the closely analogous 2-methyl*cyclo*hexylamines (Skita, *Ber.*, 1923, **56**, 1014). The base obtained by reduction of 2-ethyl*cyclo*hexanone oxime with sodium and ethyl alcohol, or by the superior method of catalytic reduction with Raney nickel in saturated alcoholic ammonia, the latter to reduce secondary amine formation (cf. *Org. Synth.*, 1943, **23**, 72), we therefore regard as *trans*-ethyl*cyclo*hexylamine (II, R = H). It is a colourless liquid rapidly converted in air into a white mass of carbonate, but it was characterised by three crystalline derivatives, the *picrate* (m. p. 198—199°), *benzenesulphonamide* (m. p. 131°), and *trimethylammonium iodide* (m. p. 182°), all of which differ from the corresponding derivatives of perhydroindole (v. Braun *et al.*, *loc. cit.*). Methylation to the tertiary amine was effected by the convenient method of Sommelet and Farrand (*Bull. Soc. chim.*, 1924, **35**, 446; see also Clarke, Gillespie, and Weisshaus, *J. Amer. Chem. Soc.*, 1933, **55**, 4571), *viz.*, heating with formaldehyde and formic acid. The resulting *trans*-*N*-dimethyl-2-ethyl*cyclo*hexylamine (II, R = Me), a colourless liquid unaffected by exposure to air, gave with methyl iodide the salt, m. p. 182°, already prepared from the *trans*-primary base.

For the preparation of the *cis*-series, 2-ethyl*cyclo*hexanone oxime was heated under pressure with ammonium formate (Leuckardt reaction). The crude *N*-formyl compound was hydrolysed, and the amine purified through its *benzenesulphonamide*. Hydrolysis of this derivative with concentrated hydrochloric acid in a sealed tube afforded *cis*-2-ethyl*cyclo*hexylamine (II, R = H), like the *trans*-isomer, a colourless oil rapidly forming in the air a solid carbonate. The *cis*-amine was also obtained by catalytic reduction of the oxime in acid solution and characterised by the *benzenesulphonamide* (m. p. 161°) and *picrate* (m. p. 189°). Methylation with formaldehyde and formic acid gave in good yield, *cis*-*N*-dimethyl-2-ethyl*cyclo*hexylamine, which afforded a crystalline *methiodide* (m. p. 231°). The m. p.'s recorded by v. Braun for the derivatives of perhydroindole are: benzenesulphonamide 120°, picrate 189—190°, and trimethylammonium iodide 231°. No definite reason for the divergence in the sulphonamide m. p.'s can be offered, but the correspondence between the other two pairs of derivatives may be taken to indicate that perhydroindole is *cis*-2-ethyl*cyclo*hexylamine. This apparently exceptional formation of a *cis-cyclo*hexylamine under *neutral* conditions can, however, be reconciled with the Skita rule if it is allowed that the perhydroindole is produced through the octahydro-compound, which, for reasons already indicated, very probably has the *cis*-structure.

Because they are unaffected by exposure to the air, the *cis*- and *trans*-dimethyl*cyclo*hexylamines are more

suitable than the corresponding primary amines for physical measurements, and the refractive index and density determinations (made by Dr. Strauss of this Laboratory) are recorded in the experimental section. The relationship between the two series is in accord with the stereochemical structures assigned on the basis of Skita's conclusions.

Owing to lack of suitable high-pressure apparatus, when this work was begun we had great difficulty in the preparation of octahydroindole by Raney nickel hydrogenation in *cyclo*hexane or dioxan. By using ethanol as a solvent, dihydroindole was readily obtained, but on raising the temperature to effect further reduction, *N*-alkylation also occurred (cf. Winans and Adkins, *J. Amer. Chem. Soc.*, 1932, **54**, 306) and a quantitative yield of N-*ethyloctahydroindole* resulted. Reduction in methanol likewise afforded N-*methyloctahydroindole*, and the crystalline *methiodide* of this base was used for the Hofmann degradation.

Somewhat surprisingly, in view of the results with decahydroquinoline and 2-methyloctahydroindole (Fujise, *loc. cit.*), decomposition of the quaternary hydroxide ruptured the bond by which the nitrogen atom is attached to the *cyclo*hexane ring, and a methine base was obtained, subsequently identified as a β-*dimethylaminoethyl*cyclo*hexene*, $C_6H_9 \cdot CH_2 \cdot CH_2 \cdot NMe_2$, from its reduction to β-*dimethylaminoethyl*cyclo*hexane* (III). By methylating β-phenylethylamine to the *N*-dimethyl derivative, which was then completely hydrogenated over Raney nickel, the amine (III) was synthesised, and a comparison of the *picrate*, *picrolonate*, and *methiodide* with the corresponding salts of the hydroindole exhaustive methylation product definitely established the identity of the latter.

Experimental.

Ethyl cyclo*Hexanone*-2-*carboxylate* (Kötz, *Annalen*, 1907, **358**, 198).—The yield of this ester, b. p. 106°/11 mm., obtained by Kötz (50%) is raised to 61% by heating the *cyclo*hexanoneglyoxylic ester at 140° under reduced pressure in a flask packed with glass wool (Found: C, 63·4; H, 8·2. Calc. for $C_9H_{14}O_3$: C, 63·5; H, 8·2%).

2-*Ethyl*cyclo*hexanone* (cf. Vavon and Mitchovitch, *loc. cit.*).—The *cyclo*hexanonecarboxylate (93 g.) was heated with powdered sodium (12·6 g.) in refluxing benzene (500 c.c.) for 3 hours. After the addition of ethyl iodide (79 g.) and a further 8 hours' heating, the benzene layer was washed, dried, and distilled, giving ethyl 2-ethyl*cyclo*hexanone-2-carboxylate (93 g., 86%), b. p. 122—124°/14 mm. By refluxing with hydrochloric acid (500 c.c. of 20%) and occasionally distilling the alcohol produced, the ester (87 g.) was largely hydrolysed in 16 hours. Ether extraction of the diluted solution gave the colourless ketone (41 g.), b. p. 73·5—74·5°/35 mm., of which the 2 : 4-*dinitrophenylhydrazone* crystallised from alcohol in red needles, m. p. 162° (Found: C, 54·6; H, 6·0. $C_{14}H_{18}O_4N_4$ requires C, 54·9; H, 5·9%).

trans-2-*Ethyl*cyclo*hexylamine*.—(i) From the ethyl*cyclo*hexanone (10 g.), hydroxylamine hydrochloride (9 g.), and sodium acetate in hot aqueous alcohol, an oxime (10 g.) was prepared, b. p. 111°/11 mm., m. p. *ca.* 35—40° (Vavon and Mitchovitch, *loc. cit.*, give m. p. 60°). It was dissolved in refluxing absolute alcohol (100 c.c.) to which sodium (8 g.) was added in portions. At the end of the reaction the cold solution was acidified with hydrochloric acid, and the alcohol removed under reduced pressure. The residue was strongly basified with potassium hydroxide, and the amine (6·7 g.) isolated by ether as a colourless oil, b. p. 65°/17 mm., which rapidly became covered by a white film of carbonate. Alcoholic picric acid gave a *picrate* (yield 80%), m. p. 195—198°, which on recrystallisation from alcohol formed yellow, flat prisms, m. p. 198—199° (decomp.) (Found: C, 47·4; H, 5·7. $C_8H_{17}N,C_6H_3O_7N_3$ requires C, 47·2; H, 5·6%).

With benzenesulphonyl chloride, a pyridine solution of the base afforded a *benzenesulphonamide*, crystallising in masses of minute needles, m. p. 131° (Found: C, 62·8; H, 7·7. $C_{14}H_{21}O_2NS$ requires C, 62·9; H, 7·8%). *trans*-2-Ethyl*cyclo*hexylamine reacted vigorously with methyl iodide, and the resulting *N-dimethyl-2-ethyl*cyclo*hexylamine methiodide* separated from ethyl acetate in colourless, short prisms, m. p. 182° (Found: I, 42·9. $C_{11}H_{24}NI$ requires I, 42·9%).

(ii) The oxime (11 g.), dissolved in alcohol saturated with ammonia, was hydrogenated over Raney nickel for 3 hours at 130° at an initial pressure of 83 atm. The filtered solution was acidified with hydrochloric acid, the alcohol evaporated, and the base liberated by alkali was extracted with ether and distilled. The product (7·8 g., 79%) had b. p. 149—151°/745 mm., and was identified as *trans*-2-ethyl*cyclo*hexylamine by the benzenesulphonamide of m. p. and mixed m. p. 131°.

trans-N-*Dimethyl-2-ethyl*cyclo*hexylamine*.—The primary amine (5·8 g.), dissolved in formic acid (4·2 g. of 100%) and aqueous formaldehyde (7·9 c.c. of 35%), was heated on a steam-bath, carbon dioxide being rapidly evolved. After 1 hour the solution was boiled for 2—3 minutes, and the base liberated by addition of potassium hydroxide was extracted with ether. Traces of primary and secondary amines were eliminated by nitrous acid, leaving the purified *N-dimethyl-2-ethyl*cyclo*hexylamine* (5·5 g.), b. p. 187·5—188·5°/745 mm., d_{20} 0·8464; n_{20} 1·4573 (Found: N, 8·8. $C_{10}H_{21}N$ requires N, 9·0%). With methyl iodide the metho-salt already prepared from the primary base was obtained, m. p. and mixed m. p., 182°.

cis-2-*Ethyl*cyclo*hexylamine*.—(i) 2-Ethyl*cyclo*hexanone (11 g.) was heated with ammonium formate (16·5 g.) in a sealed tube at 210° for 12 hours. Water was then added, and by ether extraction the ethyl*cyclo*hexylformamide (10 g.), b. p. 145—155°/12 mm., was isolated, and was hydrolysed by refluxing with alcoholic potassium hydroxide (15 g. in 110 c.c.). Evaporation of the acidified solution and ether extraction of the basified residue gave the crude amine, and this was heated at 100° for 10 minutes with pyridine (21 c.c.) and benzenesulphonyl chloride (12·5 g.). After 3 crystallisations from alcohol, the *benzenesulphonamide* formed colourless, square tablets, m. p. 161° (Found: C, 62·7; H, 7·7. $C_{14}H_{21}O_2NS$ requires C, 62·9; H, 7·8%).

The amide (5·5 g.) was heated with concentrated hydrochloric acid (15 c.c.) in a sealed tube at 175° for 12 hours. The tarry ether-soluble layer was removed and the aqueous solution basified, thus liberating *cis*-2-ethyl*cyclo*hexylamine, a colourless mobile oil, b. p. 64°/16 mm., rapidly covered by a white crust of carbonate on exposure to the air. The *picrate*, m. p. 189°, separated from water in long yellow needles (Found: C, 47·3; H, 5·9. $C_8H_{17}N,C_6H_3O_7N_3$ requires C, 47·2; H, 5·6%).

(ii) 2-Ethyl*cyclo*hexanone oxime (8·5 g.) in alcoholic solution (50 c.c.) containing concentrated hydrochloric acid (8 c.c.) was hydrogenated over palladised charcoal catalyst at atmospheric pressure for 3 days. Water was added, unchanged oxime recovered by ether extraction after removal of alcohol under reduced pressure, and the base liberated by alkali. The *cyclo*hexylamine (1 g.) distilled at 69—73°/20 mm., leaving a large residue, and was identified by the benzenesulphonamide, m. p. and mixed m. p. 161°.

cis-N-*Dimethyl-2-ethyl*cyclo*hexylamine*.—A solution of the primary amine (0·8 g.) in aqueous formaldehyde (1·3 c.c. of 35%) and formic acid (0·62 g.) was heated at 100° until effervescence ceased (1 hour), and then refluxed for a further 5 minutes. The *cis*-amine (0·7 g.) obtained by ether extraction of the cooled and basified solution had b. p. 82—83°/20 mm., d_{23} 0·8657, n_{20} 1·4585. The action of methyl iodide in dry ether precipitated the base *methiodide*, which crystal-

lised from acetone–ether in colourless needles, m. p. 231° (decomp.) (Found: C, 44·7; H, 8·2; N, 4·8. $C_{11}H_{24}NI$ requires C, 44·4; H, 8·1; N, 4·7%).

1-*Ethyloctahydroindole*.—Indole (1 mol.) was hydrogenated in *cyclo*hexane or dioxan (15 mols.) at 100—110 atm. in presence of Raney nickel. With increasing temperature, *i.e.*, up to 150—160°, 1 mol. of hydrogen was absorbed, corresponding to the formation of dihydroindole, but thereafter no observable reduction occurred until, at 200°, further very slow absorption took place. Fractionation of the product and purification through a picrate (m. p. *ca.* 130—135°) gave a small quantity of a base which after distillation yielded *octahydroindole picrolonate*, crystallising from ethanol in yellow rhombic tablets, m. p. 220° with subsequent darkening (Found: C, 55·7; H, 5·4. $C_8H_{15}N,C_{10}H_8O_5N_4$ requires C, 55·5; H, 5·9%).

The reduction of indole in ethanol solution at 100—110° and a maximum pressure of 90—100 atm. gave the theoretical amount of 2 : 3-dihydroindole, b. p. 89—94°/10 mm. (Found: C, 80·4; H, 8·0; N, 11·8. Calc. for C_8H_9N: C, 80·6; H, 7·6; N, 11·8%), identified by the picrate, m. p. 174°. Further reduction, which was accompanied by *N*-ethylation, required a temperature of 150—160°, and the yield of 1-*ethyloctahydroindole*, a colourless oil of b. p. 68°/11 mm., was quantitative (Found: C, 78·1; H, 12·4; N, 9·8. $C_{10}H_{19}N$ requires C, 78·4; H, 12·4; N, 9·1%). The amine *picrate* crystallised from alcohol in fine, bright yellow prisms, m. p. 147—150° (Found: N, 15·0. $C_{10}H_{19}N,C_6H_2O_7N_3$ requires N, 14·7%).

1-*Methyloctahydroindole*.—A solution of indole (10 g.) in methyl alcohol (100 c.c.) was hydrogenated at 170° and an initial pressure of 80 atm. with a Raney nickel catalyst. The filtered and acidified solution was evaporated, and extraction of the basified product gave 1-*methyloctahydroindole* (9 g.) as a colourless oil, b. p. 178—179°/757 mm. (Found: C, 77·2; H, 12·2. $C_9H_{17}N$ requires C, 77·7; H, 12·2%). The base *methiodide*, which was precipitated at room temperature from a solution of 1-methyloctahydroindole in ether containing methyl iodide, crystallised from acetone–ether in long, colourless needles, m. p. 201° (Found: I, 45·0. $C_{10}H_{20}NI$ requires I, 45·2%). On warming the iodide with saturated alcoholic picric acid, a *methopicrate* was obtained, which crystallised from alcohol in long, yellow needles, m. p. 194° (Found: C, 49·6; H, 5·8. $C_{16}H_{22}O_7N_4$ requires C, 50·2; H, 5·8%).

β-*Dimethylaminoethyl*cyclo*hexene*.—Dimethyloctahydroindolinium iodide (12·5 g.) was dissolved in water (60 c.c.) and shaken for 1 hour with silver oxide, freshly prepared from silver nitrate (10 g.) and sodium hydroxide (2·4 g.). The filtered solution was evaporated at 50°, and the syrupy residue of quaternary hydroxide decomposed by heating under reduced pressure at 90—100°. The base distilling was taken up in ether, and the solution dried and evaporated, β-*dimethylaminoethyl*cyclo*hexene* being isolated from the residue (3·6 g.) as a colourless oil, b. p. 84°/14 mm., which decolourised bromine water and aqueous potassium permanganate (Found: C, 77·8; H, 12·7. $C_{10}H_{19}N$ requires C, 78·5; H, 12·4%). The amine *picrolonate* crystallised from ethanol in yellow needles, m. p. 184—185° (Found: C, 57·4; H, 6·5. $C_{10}H_{19}N,C_{10}H_8O_5N_4$ requires C, 57·6; H, 6·5%). Addition of excess methyl iodide to the base dissolved in ether precipitated the *methiodide*, which separated from acetone–ether in microscopic rhombs, m. p. 226—227° (Found: C, 44·7; H, 7·7. $C_{11}H_{22}NI$ requires C, 44·7; H, 7·5%).

β-*Dimethylaminoethyl*cyclo*hexane*.—The dimethylaminoethyl*cyclo*hexene (2·6 g.) was hydrogenated in the form of its hydrochloride in ethanol solution (50 c.c.) over palladised charcoal at atmospheric pressure. After filtration, the solution was evaporated, and the residue basified and extracted in ether. β-Dimethylaminoethyl*cyclo*hexane (2·3 g.) was thus isolated as an oil, b. p. 83°/15 mm., characterised by its *picrolonate*, which crystallised in yellow needles from ethanol, m. p. 191° (Found: C, 57·2; H, 7·0. $C_{10}H_{21}N,C_{10}H_8O_5N_4$ requires C, 57·3; H, 6·9%). The picrate, yellow needles, m. p. 150°, from ethanol, and methiodide, colourless prisms, m. p. 224°, from acetone–ether, were also prepared.

Dimethyl-β-phenylethylamine.—Benzyl cyanide (50 g.), dissolved in saturated alcoholic ammonia (500 c.c.), was hydrogenated, initially at 90 atm., over Raney nickel for 7 hours at 110°. After acidification of the filtered solution with hydrogen chloride, water was added to dissolve the crystalline precipitate, and the alcohol distilled under reduced pressure. The aqueous residue was then extracted with ether and basified, whereupon β-phenylethylamine was liberated, and when isolated with ether the pure base distilled as a colourless liquid, b. p. 89·5—91°/91 mm., characterised by the picrate, m. p. 169°, in agreement with the recorded values.

To a solution of the β-phenylethylamine (24·2 g.) in formic acid (18·5 g.), formaldehyde (35 c.c. of 35%) was added, and the mixture warmed on a steam-bath for 1 hour. When the reaction had been completed by brief refluxing, the tertiary amine was isolated by addition of alkali and ether extraction. The product (21 g.) was a colourless oil, b. p. 203—205°, and the picrate had m. p. 135° (Decker and Becker, *Ber.*, 1912, **45**, 2407, record m. p. 133—134°) (Found: C, 50·7; H, 4·7. Calc. for $C_{16}H_{18}O_7N_4$: C, 50·8; H, 4·8%).

Reduction of the tertiary amine (10 g.), dissolved in methanol (100 c.c.), over Raney nickel for 16 hours at 200° with an initial hydrogen pressure of 83 atm. was accompanied by extensive hydrogenolysis. However, after filtration and evaporation of the acidified solution, which was then basified and extracted with ether, β-dimethylaminoethyl*cyclo*hexane (1 g.) was obtained as a colourless liquid distilling at 87—88°/21 mm. Alcoholic picric acid afforded the *picrate*, crystallising from ethanol in long, yellow needles, m. p., alone or mixed with the salt obtained from *N*-methyloctahydroindole by the Hofmann degradation, 150° (Found: C, 50·3; H, 6·1. $C_{10}H_{21}N,C_6H_3O_7N_3$ requires C, 50·5; H, 6·2%). Similarly, the *methiodide*, which separated from acetone–ether in fine, colourless needles, was identified with the corresponding salt from the same source by its m. p. and mixed m. p. of 219—220° (Found: C, 44·6; H, 8·1; N, 4·9. $C_{11}H_{24}NI$ requires C, 44·4; H, 8·1; N, 4·7%).

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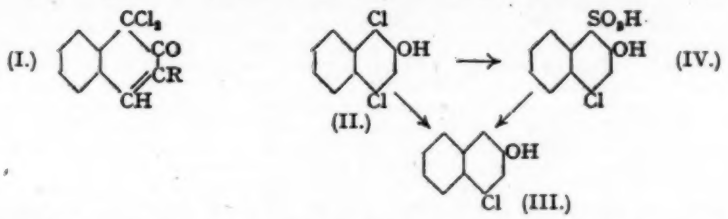
73. *The Chlorination of β-Naphthol and Ethyl 2-Hydroxy-3-naphthoate in Presence of Sodium Acetate. 4-Chloro-β-naphthol and its Derivatives.*

By HAROLD BURTON.

The conversion of 1 : 1-dichloro-2-keto-1 : 2-dihydronaphthalene (I, R = H) into 1 : 4-dichloro-β-naphthol (II) by hydrogen chloride in acetic acid (Fries and Schimmelschmidt, *Annalen*, 1930, **484**, 295) has been modified to give a 45—50% overall yield from β-naphthol. Attempted application of the method to ethyl 2-hydroxy-3-naphthoate was not successful.

CHLORINATION of β-naphthol in presence of acetic acid and sodium acetate was shown by Fries and Schimmelschmidt (*loc. cit.*) to give 1 : 1-dichloro-2-keto-1 : 2-dihydronaphthalene (I, R = H), which, under the influence of hydrogen chloride in acetic acid, was converted into 1 : 4-dichloro-β-naphthol (II), a com-

pound first obtained in poor yield by Zincke (*Ber.*, 1888, **21**, 3387) by reduction of 1 : 1 : 3 : 4-tetrachloro-2-keto-1 : 2 : 3 : 4-tetrahydronaphthalene, and later by Armstrong and Rossiter (*Proc.*, 1891, **7**, 32) by the

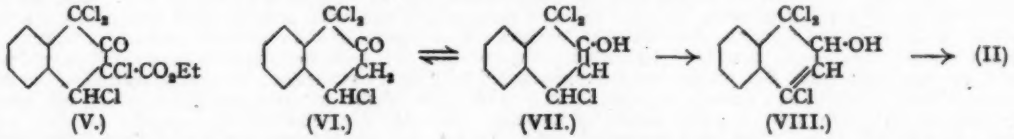


action of sulphuryl chloride on β-naphthol. Investigation of the former method has led to (II) in 45—50% yield from the β-naphthol used.

The 1-chlorine atom of (II) is not very reactive and is not removed by the usual acid or alkaline reducing agents; with stannous chloride in acetic acid–hydrogen chloride at 100° under pressure, as recommended by Fries and Schimmelschmidt (*loc. cit.*), conversion into 4-chloro-β-naphthol (III) occurs. Prolonged treatment of (II) with sodium sulphite in boiling aqueous alcohol gave 15% of *4-chloro-β-naphthol-1-sulphonic acid* (IV), the sulphonic acid group of which was readily eliminated under the influence of boiling dilute sulphuric acid, thus giving (III) by an alternative route. *4-Chloro-2-hydroxy-1-naphthaldehyde* could not be obtained from (III) by means of *N*-methylformanilide and phosphoryl chloride, but was presumably obtained (see Experimental) by the Reimer–Tiemann reaction.

Chlorination of 2-hydroxy-3-naphthoic acid under conditions similar to those used for β-naphthol gave a product which, as expected of a β-ketonic acid, rapidly decomposed. Ethyl 2-hydroxy-3-naphthoate, on the other hand, afforded the stable *ethyl 1 : 1-dichloro-2-keto-1 : 2-dihydro-3-naphthoate* (I, R = CO_2Et), which was not rearranged smoothly by acetic acid–hydrogen chloride. The use of ethyl-alcoholic hydrogen chloride gave ethyl 1-chloro-2-hydroxy-3-naphthoate as the main identifiable product (*ca.* 20%), together with much amorphous material, and a small amount (4%) of a *dichlorohydroxynaphthoic acid* which might well be the 1 : 4-dichloro-derivative, although an attempt to obtain (II) from it by decarboxylation was inconclusive. Further chlorination of ethyl 2-hydroxy-3-naphthoate or of the dichloroketo-ester gave *ethyl 1 : 1 : 3 : 4-tetrachloro-2-keto-1 : 2 : 3 : 4-tetrahydro-3-naphthoate* (V), but attempted reductions (compare Zincke, *loc. cit.*) of this to the 1 : 4-dichloro-derivative were unsuccessful; ethyl 1-chloro-2-hydroxy-3-naphthoate was again the main identifiable product.

The relatively facile conversion of (I, R = H) but not of (I, R = CO_2Et) into a 1 : 4-dichloro-β-naphthol suggests that the first stage in the process might be the addition of hydrogen chloride across the 3 : 4-double linking to give 1 : 1 : 4-trichloro-2-keto-1 : 2 : 3 : 4-tetrahydronaphthalene (VI). Such a compound could enolise in one direction only, namely to (VII), and if this underwent a prototropic change to the trichlorocarbinol (VIII), followed by loss of hydrogen chloride, 1 : 4-dichloro-β-naphthol would result.



Such a mechanism for the action of hydrogen bromide on (I, R = H) is not applicable, since the final product is 1-chloro-6-bromo-β-naphthol. In this case it is probable that bromine chloride is an intermediate (compare Fries and Schimmelschmidt, *loc. cit.*).

Alternatively, 1 : 4-elimination of hydrogen chloride from (VI) would give (II) (in its ketonic form) directly.

Experiments to test the inter- or intra-molecular nature of the rearrangement are not easy to devise. The choice of a readily chlorinated compound to decide whether the reaction is intermolecular, *viz.*, $\cdot CCl_2\cdot CO\cdot + HCl \longrightarrow \cdot CCl{:}C(OH)\cdot + Cl_2$, is very limited. The use of an amine (*e.g.*, aniline) is impracticable, since the concentration of hydrogen chloride is so high that the base must be largely or wholly removed from solution as the hydrochloride. The use of a phenol overcomes this objection, but condensation of the phenol with the initial reactant is not precluded. It has been found that when the change (I, R = H) ⟶ (II) is carried out in presence of phenol itself, the yield of (II) is reduced but the formation of chlorophenol could not be detected. Traces of unchanged phenol may have been present in the reaction mixture, which after separation of the 1 : 4-dichloro-β-naphthol in the usual manner (see Experimental), contained a large amount of a tarry product soluble in aqueous sodium hydroxide. It must be concluded that almost the whole of the phenol had undergone condensation. The mechanism of the rearrangement thus remains obscure.

The production of 1 : 4-dichloro-β-naphthol from β-naphthol and sulphuryl chloride (Armstrong and Rossiter, *loc. cit.*) undoubtedly involves the intermediate production of 1 : 1-dichloro-2-keto-1 : 2-dihydronaphthalene, which is now shown to be produced in small but definite amount from β-naphthol and 2·5 molecules of the chloride.

Experimental.

1 : 1-*Dichloro*-2-*keto*-1 : 2-*dihydronaphthalene* (I, R = H).—The procedure of Fries and Schimmelschmidt (*loc. cit.*) was modified as follows. A solution of β-naphthol (72 g.; recrystallised from benzene) and crystalline sodium acetate (200 g.) in glacial acetic acid (400 c.c.) was stirred, cooled in ice, and treated with chlorine (71 g.) during not less than 2½ hours (a shorter time causes production of tar). A distinct colour change was noted when the total weight of chlorine had been absorbed. After 15 minutes, a small amount was poured on ice and stirred until solidification occurred; the remainder of the solution was then added. The mixture was stirred for 45 minutes, the solid filtered off, washed with water, ground into a paste with acetic acid, refiltered, and finally washed with a little light petroleum (b. p. 80—100°). This material (*A*) was used for conversion into 1 : 4-dichloro-β-naphthol. Further purification (as above) and recrystallisation of this product from light petroleum (b. p. 40—60°) gave massive prisms, m. p. 48—50°, unaltered by further crystallisation. Fries and Schimmelschmidt (*loc. cit.*) give m. p. 54°.

1 : 4-*Dichloro*-β-*naphthol* (II).—The material (*A*) was shaken vigorously in a wide-mouthed bottle with a saturated solution (80 c.c.) of hydrogen chloride in glacial acetic acid for 2—3 minutes. The mixture was then cooled in ice-water, stirred, and dry hydrogen chloride slowly passed in for 30 minutes. The bottle was stoppered and kept in a cool place for *ca.* 18 hours. The resulting solid was filtered off, washed repeatedly with successive small amounts of acetic acid until the filtrate was nearly colourless, and finally with light petroleum (b. p. 80—100°). Recrystallisation from light petroleum (b. p. 80—100°; 300 c.c.; little charcoal) gave 50±2 g. of 1 : 4-dichloro-β-naphthol, m. p. 122—123°.

When this experiment (see p. 281) was carried out in the presence of phenol (23·5 g.), the yield of recrystallised 1 : 4-dichloro-β-naphthol was 25 g. Neutralisation of the filtrate with sodium carbonate and steam-distillation gave a further quantity of the dichloronaphthol as the sole volatile product.

4-*Chloro*-β-*naphthol*-1-*sulphonic Acid* (IV).—A mixture of 1 : 4-dichloro-β-naphthol (10·7 g.), crystalline sodium sulphite (25·2 g.), water (250 c.c.), and 95% alcohol (150 c.c.) was boiled for 72 hours. On cooling, unchanged dichloronaphthol (5·5 g.) crystallised. Evaporation of the alcohol and extraction of the aqueous residue with ether gave a further 2·6 g. of dichloronaphthol. The aqueous solution was evaporated to small bulk, acidified with sulphuric acid, and boiled to expel sulphur dioxide. The *sulphonic acid* (2 g.) crystallised, and after being washed with water and a little alcohol, was recrystallised from water, separating in nearly colourless plates, which sintered at *ca.* 200° but did not melt up to 260°, and appeared to contain 0·5 mol. of water of crystallisation (not lost at 100° in a vacuum) (Found: Cl, 13·2; S, 11·9. $C_{10}H_7O_4ClS,0{\cdot}5H_2O$ requires Cl, 13·3; S, 12·0%).

4-*Chloro*-β-*naphthol* (III).—(*a*) The above sulphonic acid (5·2 g.), water (150 c.c.), and concentrated sulphuric acid (50 c.c.) were boiled for 20 minutes. On cooling, the chloronaphthol (3·2 g.) crystallised; recrystallisation from light petroleum (b. p. 80—100°) gave needles, m. p. 102—103°.

(*b*) A mixture of 1 : 4-dichloro-β-naphthol (15 g.), stannous chloride dihydrate (70 g.), and 300 c.c. of a saturated solution of hydrogen chloride in acetic acid was heated in a pressure bottle in a boiling water-bath for 8 hours. The solution was poured, when cold, into ice-water, and the crystalline material (12 g.), m. p. 95°, filtered off. (If this product had m. p. 83—87°, the above treatment had to be repeated, indicating incomplete removal of the 1-chlorine atom.) Recrystallisation from light petroleum (b. p. 80—100°) gave nearly colourless, silken needles (9·2 g.), m. p. 103—104°, unchanged by admixture with a specimen prepared as in (*a*).

4-Chloro-β-naphthol could not be obtained from the dichloronaphthol by means of tin and a mixture of boiling concentrated hydrochloric and acetic acids or by zinc dust in boiling aqueous potassium hydroxide.

4-Chloro-β-naphthol was characterised as the acetate, colourless plates from light petroleum (b. p. 40—60°), m. p. 58—59° (Hodgson and Birtwell, J., 1943, 468, give m. p. 56°) (Found: Cl, 16·1. Calc. for $C_{12}H_9O_2Cl$: Cl, 16·1%), and as the *benzoate*, colourless needles from alcohol, m. p. 83—84° (Found: C, 72·0; H, 4·0; Cl, 12·75. $C_{17}H_{11}O_2Cl$ requires C, 72·2; H, 3·9; Cl, 12·6%).

4-*Chloro*-2-*hydroxy*-1-*naphthaldehyde*.—A solution of 4-chloro-β-naphthol (25 g.) and sodium hydroxide (40 g.) in water (100 c.c.) and alcohol (80 c.c.) was heated under reflux to 65°, and chloroform (20 g.) added dropwise. A deep green colour, changing to brown, developed and the temperature rose to 75° and then fell to 70°. After 30 minutes, the alcohol was removed by distillation, and the aqueous residue acidified with concentrated hydrochloric acid. The solid residue (29 g.) obtained from the dried ethereal extract was dissolved in the minimum amount of boiling alcohol; on cooling, the aldehyde (6·5 g.), m. p. 118°, separated. Evaporation of the alcoholic filtrate gave much purple material, from which unchanged 4-chloro-β-naphthol (4 g.) was extracted with light petroleum. Recrystallisation of the aldehyde from alcohol or acetic acid gave a colourless product, m. p. 118—119° (slight previous shrinking), which was apparently not homogeneous but could not be fractionated by alcohol. The *aldehyde* [Found: (i) C, 64·0; H, 3·5; Cl, 17·6; (ii) C, 64·1; H, 3·5; Cl, 17·5. $C_{11}H_7O_2Cl$ requires C, 63·9; H, 3·4; Cl, 17·2%] does not react with sodium bisulphite; it gives the characteristic yellow colour of an *o*-hydroxy-aldehyde with aqueous ammonia.

An attempt to obtain the aldehyde from 4-chloro-β-naphthol (8·6 g.), *N*-methylformanilide (17 g.), and phosphoryl chloride (21 g.) at 75—78° for 2 hours was unsuccessful. The product gave hardly any precipitate with semicarbazide acetate, whereas the above aldehyde reacts readily to give the insoluble semicarbazone, which does not melt up to 280°.

Ethyl 1 : 1-*Dichloro*-2-*keto*-1 : 2-*dihydro*-3-*naphthoate* (I, R = CO_2Et).—A solution of ethyl 2-hydroxy-3-naphthoate (54 g.) and crystalline sodium acetate (100 g.) in acetic acid (600 c.c.) was treated in the cold with chlorine (36 g.) during 1½ hours. The solution was poured on ice (450 g.), and the mixture stirred. The resulting solid (70 g.), m. p. *ca.* 70°, was dried, and recrystallised from light petroleum (b. p. 60—80°), forming colourless prisms, m. p. 85—86° (Found: Cl, 24·8. $C_{13}H_{10}O_3Cl_2$ requires Cl, 24·9%). The *ester* is more stable than 1 : 1-dichloro-2-keto-1 : 2-dihydronaphthalene; it liberates iodine from potassium iodide in acetic acid and is reduced by sulphur dioxide in aqueous-alcoholic solution to ethyl 1-chloro-2-hydroxy-3-naphthoate, m. p. 113—114° (from alcohol).

Attempted Rearrangement of Ethyl 1 : 1-*Dichloro*-2-*keto*-1 : 2-*dihydro*-3-*naphthoate*.—Solutions of the ester in acetic acid saturated with hydrogen chloride contained unchanged material (potassium iodide test) after 72 hours. After 14 days, the only crystalline product isolable after dilution with water was ethyl 1-chloro-2-hydroxy-3-naphthoate, m. p. 111—112°, identified by hydrolysis to the free acid, m. p. 230°.

The crude ester (70 g.), suspended in absolute alcohol (200 c.c.), was treated with dry hydrogen chloride until it dissolved, and the mixture was then cooled in ice and saturated with hydrogen chloride (if solid separated during this process, the mixture was removed from the cooling bath until redissolution occurred). After 18 hours at room temperature, yellow needles of ethyl 1-chloro-2-hydroxy-3-naphthoate (12 g.) had separated. Evaporation of the filtrate to about one-third of its bulk gave a further 4 g. of this ester, m. p. 111—112°. The new filtrate was hydrolysed with sodium hydroxide (50 g. in 200 c.c. of water) during 3 hours and then acidified with concentrated hydrochloric acid. The resulting air-dried solid (35 g.) was extracted with three successive portions (100 c.c.) of benzene, and the solid which separated from the combined extracts was recrystallised from water (yield, 6 g.). Four recrystallisations from xylene then gave yellow needles (3 g.), m. p. 192—193° after slight previous softening, which appear to be a *dichloro-*

hydroxynaphthoic acid (Found : Cl, 27·5. $C_{11}H_8O_3Cl_2$ requires Cl, 27·6%). Attempted decarboxylation in boiling quinoline containing a little copper-bronze gave no crystalline product.

The above benzene extracts contained a large amount of an acid oil and a neutral resin.

Ethyl 1 : 1 : 3 : 4-*Tetrachloro*-2-*keto*-1 : 2 : 3 : 4-*tetrahydro*-3-*naphthoate* (V).—A solution of ethyl 2-hydroxy-3-naphthoate (25 g.) and crystalline sodium acetate (50 g.) in acetic acid (400 c.c.) was treated in the cold with chlorine (25 g.) during 1½ hours. The sticky product obtained by adding the mixture to ice gradually solidified; the air-dried material (40 g.), recrystallised from ligroin (b. p. 60—80°), gave colourless prisms, m. p. 73—74°, which were probably not quite pure (Found : Cl, 37·2. $C_{13}H_{10}O_3Cl_4$ requires Cl, 39·9%).

The *ester* liberated iodine from potassium iodide in acetic acid and thereby yielded ethyl 1-chloro-2-hydroxy-3-naphthoate, m. p. and mixed m. p. 113—114°. Sulphur dioxide in aqueous-alcoholic solution had no effect. Reduction of the tetrachloro-ester with stannous chloride in acetic–concentrated hydrochloric acids also gave ethyl 1-chloro-2-hydroxy-3-naphthoate. Tarry or amorphous products were obtained when the tetrachloro-ester was treated with pyridine, pyridine and sulphur dioxide, or alkali under various conditions.

Chlorination of β-Naphthol with Sulphuryl Chloride.—A mixture of β-naphthol (18 g.), sulphuryl chloride (42 g., 2·5 mols.), and dry carbon tetrachloride (50 c.c.) was warmed until reaction set in. After the initial phase (cooling in water was necessary), the mixture was heated on the steam-bath for 1 hour. The residue obtained by evaporation was kept in a vacuum desiccator, and a small amount of crystalline material separated. Recrystallisation from light petroleum (b. p. 40—60°) gave 1 : 1-dichloro-2-keto-1 : 2-dihydronaphthalene, m. p. and mixed m. p. 48—50°.

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THE UNIVERSITY, LEEDS, 2. [*Received, November 23rd*, 1944.]

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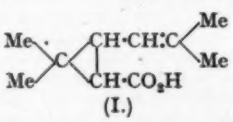
74. *Experiments on the Synthesis of the Pyrethrins. Part I. Synthesis of Chrysanthemum Monocarboxylic Acid.*

By (MISS) I. G. M. CAMPBELL and STANLEY H. HARPER.

Addition of ethyl diazoacetate to βε-dimethyl-$\Delta^{\beta\delta}$-hexadiene gave the ethyl esters of *dl-cis-* and *dl-trans*-2 : 2-dimethyl-3-*iso*butenyl*cyclo*propane-1-carboxylic acids. Resolution of the crystalline dl-trans-*acid* by means of the *quinine* salt gave the *l-trans*-acid ($[\alpha]_D$ − 14·0°) in a state of optical purity. This acid is the optical enantiomorph of chrysanthemum monocarboxylic acid ($[\alpha]_D$ + 14·2°), the acidic component of pyrethrin I, which is therefore *d-trans*-2 : 2-dimethyl-3-*iso*butenyl*cyclo*propane-1-carboxylic acid. The *quinine* salt of the *d-trans*-acid could not be obtained pure. However, by fractional crystallisation of the *p*-phenylphenacyl ester of the recovered acid ($[\alpha]_D$ + 8·0°), the p-*phenylphenacyl* ester of the *d-trans*-acid was obtained optically pure and identical with that prepared from the natural acid.

DURING 1910—1916 Staudinger and Ruzicka elucidated the main structural features of pyrethrins I and II, the active principles of Dalmatian pyrethrum flowers, *Chrysanthemum cinerariifolium*. These were shown to be esters of the keto-alcohol, pyrethrolone, with chrysanthemum mono- and di-carboxylic acids respectively. Chrysanthemum monocarboxylic acid, separated by reason of its volatility in steam, was an optically active liquid acid, $C_{10}H_{16}O_2$. On ozonisation the acid gave *l-trans*-caronic acid and acetone, establishing its structure as (I). Likewise the dicarboxylic acid, an optically active crystalline acid, $C_{10}H_{14}O_4$, gave on ozonisation *l-trans*-caronic acid and pyruvic acid, establishing its structure as (II).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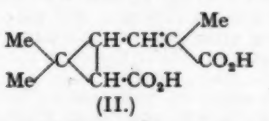
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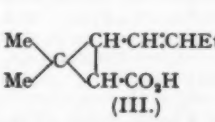

(III.)

In the interval preceding the publication of Staudinger and Ruzicka's work (*Helv. Chim. Acta*, 1924, **7**, 177, 201) Yamamoto (*J. Tokyo Chem. Soc.*, 1919, **40**, 126; *J. Chem. Soc. Japan*, 1923, **44**, 311, 1070) independently isolated from Japanese pyrethrum flowers, *C. cinerariifolium*, an optically inactive liquid acid, pyrethronic acid, $C_{10}H_{16}O_2$. On ozonisation the acid gave *dl-trans*-caronic acid and propaldehyde, establishing its structure as (III). The difference in properties and structure of pyrethronic and chrysanthemum monocarboxylic acids could be explained if Japanese and Dalmatian pyrethrum contained different active principles This has, however, been disproved by Gnadinger and Corl (*J. Amer. Chem. Soc.*, 1929, **51**, 3054), who isolated pyrethrins I and II from Japanese pyrethrum.

In view of the uncertainty of the identity of chrysanthemum monocarboxylic acid and pyrethronic acid, the differing structures put forward for each, and the fact that these structures depend solely on degradative evidence, an attempt has been made to clarify the problem by synthetic methods. In view of the internal self-consistency of Staudinger and Ruzicka's structures for the mono- and the di-carboxylic acids attention has been directed in the first place to the synthesis and resolution of chrysanthemum monocarboxylic acid.

Staudinger, Muntwyler, Ruzicka, and Seibt (*Helv. Chim. Acta*, 1924, **7**, 390) attempted to synthesise chrysanthemum monocarboxylic acid by the addition of ethyl diazoacetate to βε-dimethyl-$\Delta^{\beta\delta}$-hexadiene. This hexadiene was prepared by distilling βε-dichloro-βε-dimethylhexane with soda–lime, but by modern standards the hydrocarbon was very impure. From the products of addition, followed by hydrolysis, *dl-cis*-2 : 2-dimethyl-3-*iso*butenyl*cyclo*propane-1-carboxylic acid was isolated in crystalline form in 1% yield. The *dl-trans*-acid was not isolated, but was shown to be present in the oily mother-liquor from the *dl-cis*-acid,

since ozonisation gave *dl-trans*-caronic acid. No comparison was therefore possible between the natural optically active acid and the synthetic product.

Despite the lack of success of Staudinger and his collaborators it was felt that this method could be improved to become a practical route to the *dl-cis*- and *dl-trans*-acids. Through the work of Henne and his students (Henne, Chanan, and Turk, *J. Amer. Chem. Soc.*, 1941, **63**, 3474; Henne and Turk, *ibid.*, 1942, **64**, 826; Henne and Chanan, *ibid.*, 1944, **66**, 395) βε-dimethyl-$\Delta^{\beta\delta}$-hexadiene has become available in good yield and high purity by a two-step synthesis from β-methylallyl chloride. Addition of ethyl diazoacetate to the hydrocarbon at 100—125° caused immediate and vigorous reaction with evolution of nitrogen, the heat of reaction being dissipated by refluxing of excess of the hydrocarbon used as a diluent. From the product the mixed ethyl esters of *dl-cis*- and *dl-trans*-2 : 2-dimethyl-3-*iso*butenyl*cyclo*propane-1-carboxylic acids were obtained in 64% yield. This procedure has the advantage over the sealed tube method of Staudinger and his collaborators in that the yield and purity of the product were greatly improved and the preparation could be carried out with rapidity on a much larger scale. Saponification of the mixed esters gave a solid mixture of the *dl-cis*- and *dl-trans*-acids. The *dl-cis*-acid had the higher melting point (116°) and was the less soluble. It was separated from the *dl-trans*-acid by low-temperature crystallisation from ethyl acetate. The dl-trans-*acid* recovered by distillation was crystallised with difficulty from ethyl acetate owing to its high solubility and had m. p. 54°. Each acid was characterised by the preparation of derivatives, and the configurations confirmed by ozonolysis. Ozonisation of the *dl-cis*-acid gave *dl-cis*-caronic acid. Ozonisation of the *dl-trans*-acid likewise gave *dl-trans*-caronic acid; the *methyl* ester gave *monomethyl* dl-trans-*caronate*, and the *ethyl* ester gave *monoethyl* dl-trans-*caronate*.

Quinine was selected for the resolution and by fractional crystallisation from aqueous alcohol, the *quinine* salt of the *l-trans*-acid ($[\alpha]_D$ − 115·3°) was obtained pure. Decomposition with hydrochloric acid gave the *l-trans*-acid in a state of optical purity ($[\alpha]_D$ − 14·0°). It is therefore the enantiomorph of natural chrysanthemum monocarboxylic acid ($[\alpha]_D$ + 14·2°). Further proof of this was obtained by comparison of the melting points and specific rotations of the *amide*, *anilide*, and p-*phenylphenacyl* ester. The *l-trans*-acid, first obtained as a liquid, was ultimately crystallised. Although the natural acid has previously been obtained only as a liquid, on cooling and seeding with the *l-trans*-acid, the natural acid readily crystallised, m. p. 17—21°. Further crystallisation of the more soluble fractions from the salt of the *l-trans*-acid failed to give the *quinine* salt of the *d-trans*-acid in a state of purity; although a pure sample was prepared from the natural acid for comparison ($[\alpha]_D$ − 109·3°). Acid recovered from the salt of lowest rotation had ($[\alpha]_D$ + 8·0°). This was converted into the *p*-phenylphenacyl ester and fractionally crystallised from light petroleum. The less soluble fraction was the *dl*-ester, m. p. 115°; from the more soluble fraction the *d*-ester, m. p. 67°, was obtained in a state of optical purity and identical with the *p*-phenylphenacyl ester prepared from the natural acid.

Experimental.

All rotations were observed in absolute alcohol at room temperature. M. p.'s are uncorrected. Microanalyses are by Drs. Weiler and Strauss, Oxford.

βε-Dimethyl-$\Delta^{\alpha\epsilon}$-hexadiene (cf. Henne, Chanan, and Turk, *J. Amer. Chem. Soc.*, 1941, **63**, 3474).—In a 5-l. three-necked flask fitted with two double-surface condensers, a 1-l. dropping funnel, and a mercury-sealed Hershberg wire stirrer, fine magnesium turnings (48 g.; 2 atoms) were covered with dry ether (500 c.c.), and bromine (1 c.c.) added. β-Methylallyl chloride (360 g.; 4 mols.) in dry ether (750 c.c.) was then run in during 1 hour, reaction usually starting immediately, at such a rate that the refluxing ether was under control. Stirring finally became difficult owing to the separation of magnesium chloride. In one run in which the separation of the magnesium chloride was delayed, the yield of product was 20% greater than usual, but it was not found possible to control the separation of halide. After standing overnight, the reaction mass was decomposed with water (750 c.c.) and sufficient acetic acid (about 100 c.c.) to render the solution acid. The ethereal layer was separated, washed with water and sodium carbonate solution, and dried over calcium chloride. The ether was removed through a Dufton column, and the residue fractionated to give a cut, b. p. 107—116° (yield, 61—86% of the theoretical). This crude βε-dimethyl-$\Delta^{\alpha\epsilon}$-hexadiene, containing traces of halogen, was distilled over sodium; b. p. 112·0—113·5, the main fraction having b. p. 113·5° (Henne, Chanan, and Turk, *loc. cit.*, record b. p. 114·3°).

βε-Dimethyl-$\Delta^{\beta\delta}$-hexadiene (cf. Henne and Chanan, *ibid.*, 1944, **66**, 395).—6—8 Mesh activated alumina (500 g., Peter Spence and Sons) was shaken with chromic acid (50 g.) in water (250 c.c.) until absorption was complete. After the impregnated alumina had been dried at 100°, a portion was packed into a combustion tube to give a 50 × 2 cm. filling. The air was displaced with hydrogen, and reduction carried out at 425° until the catalyst had become uniformly green. For isomerisation to the conjugated diene βε-dimethyl-$\Delta^{\alpha\epsilon}$-hexadiene (515 g.) was added during 12 hours from a Hershberg funnel while the catalyst was maintained at 250—275°. The distillate, after drying over calcium chloride, was distilled over sodium through the Dufton column and a cut, b. p. 130—135°, taken. On keeping at 0° the conjugated diene crystallised in large prisms, from which the liquid impurities were decanted. βε-Dimethyl-$\Delta^{\beta\delta}$-hexadiene had b. p. 134·0° and m. p. 13° (381 g.; 75%) (Henne and Turk, *ibid.*, 1942, **64**, 826, give b. p. 134·5° and m. p. 13·94°).

Addition of Ethyl Diazoacetate to βε-Dimethyl-$\Delta^{\beta\delta}$-hexadiene (cf. Staudinger, Muntwyler, Ruzicka, and Seibt, *Helv. Chim. Acta*, 1924, **7**, 390).—βε-Dimethyl-$\Delta^{\beta\delta}$-hexadiene (88 g.; 0·80 mol.) and copper bronze (2 g.) were placed in a 500 c.c. three-necked flask, fitted with a reflux condenser, dropping funnel, and thermometer with the bulb dipping into the liquid. About 1 c.c. of ethyl diazoacetate was added, and the mixture heated until reaction commenced as shown by a steady evolution of nitrogen (temperature 100—125°). The remainder of the ethyl diazoacetate (46 g. in all; 0·40 mol.) was then added at such a rate as to maintain steady refluxing without external heating (15—20 minutes, temperature 125—130°).

The products from five such runs were bulked and fractionated by vacuum distillation. After two distillations the required ester fraction of ethyl *dl-cis*- and *dl-trans*-2 : 2-dimethyl-3-*iso*butenyl*cyclo*propane-1-carboxylates was obtained, b. p. 95—115°/12 mm. (250 g.; 64%, calculated on the ethyl diazoacetate). From the fraction, b. p. up to

75°/12 mm., βε-dimethyl-$\Delta^{\beta\delta}$-hexadiene (195 g.) was recovered by crystallisation and used for further condensations. The ester mixture (250 g.) was refluxed with potassium hydroxide (100 g.) in alcohol (1 l.) for 2 hours; insufficient potassium *cyclo*butanetetracarboxylate had then separated to warrant filtration (cf. Owen and Simonsen, J., 1932, 1424; 1933, 1225). Alcohol was distilled off, and the residue diluted with water and extracted with ether. From the aqueous layer the mixed acids separated on acidification and were taken out in ether. After removal of the ether the residue was distilled in a vacuum to give a mixture of *dl-cis-* and *dl-trans*-2 : 2-dimethyl-3-*iso*butenyl*cyclo*propane-1-carboxylic acids as a viscous oil which rapidly and completely crystallised, b. p. 143°/12 mm., 109°/1 mm. (195 g.; 91%).

The mixed acids (65 g.) were dissolved in ethyl acetate (200 c.c.) and kept at 0° to give a crop A (7 g.), m. p. 110—112°. The filtrate was cooled to − 80° to give a crop B (14 g.), m. p. 95—105°. Crops A and B after crystallisation several times from ethyl acetate (5 vols.) at room temperature gave the *dl-cis*-acid as fine cubic prisms, m. p. 113—116° (Staudinger, Muntwyler, Ruzicka, and Seibt, *loc. cit.*, give m. p. 115—116°) (Found : C, 71·4; H, 9·35; equiv., by titration, 169·2. Calc. for $C_{10}H_{16}O_2$: C, 71·4; H, 9·6%; equiv., 168·2). The dl-trans-*acid* in the filtrate from B was recovered by distillation, the viscous oil rapidly crystallising, m. p. 47—52°. The acid was very soluble but crystallised slowly from a very concentrated solution in ethyl acetate as elongated prisms up to 5 cm. in length, m. p. 54° (Found : C, 71·35; H, 9·5%; equiv. by titration, 169·2, 169·5). The *dl-trans*-acid had a marked negative heat of solution in ethyl acetate and methyl alcohol.

In later preparations the separation of the *dl-cis*-acid could not be effected so readily, prolonged fractional crystallisation from concentrated solutions in ethyl acetate at room temperature being necessary. This was facilitated by the characteristic crystalline forms of the *dl-cis-* and *dl-trans*-acids, enabling hand separation to be carried out.

The *dl-cis*-acid was characterised by the preparation of the following derivatives by standard methods : *amide*, fine needles, m. p. 93°, from light petroleum (Found : C, 71·5; H, 9·9. $C_{10}H_{17}ON$ requires C, 71·8; H, 10·2%); *N-xanthylamide* (cf. Phillips and Pitt, *J. Amer. Chem. Soc.*, 1943, **65**, 1355), plates, m. p. 142°, from dioxan–water (2 : 1) (Found : C, 79·5; H, 7·25. $C_{23}H_{21}O_2N$ requires C, 79·5; H, 7·25%); *anilide*, needles, m. p. 125°, from light petroleum (Found : C, 78·95; H, 8·6. $C_{16}H_{21}ON$ requires C, 78·95; H, 8·7%); *p-phenylphenacyl* ester, clumps of prisms, m. p. 91°, from alcohol (Found : C, 79·3; H, 7·3. $C_{34}H_{38}O_3$ requires C, 79·5; H, 7·2%); *p*-bromophenacyl ester, obtained as an oil which only slowly solidified and could not be satisfactorily recrystallised; *p*-nitrobenzyl ester, obtained as an oil which only slowly solidified. This ester was very soluble in light petroleum, crystallising on evaporation as plates, m. p. 44—45°.

Ozonisation. The *dl-cis*-acid (1 g.) in chloroform (50 c.c.) was treated with excess of ozone at 0°. The solvent was removed at room temperature in a vacuum, and the oily ozonide decomposed by warming on the steam-bath with water for 15 minutes. The solution was concentrated and allowed to crystallise. *dl-cis*-Caronic acid (368 mg.) separated slowly as brownish prisms, m. p. 174—175° with evolution of water (Perkin and Thorpe, J., 1899, **75**, 48, record 176°).

The *dl-trans*-acid was characterised by the preparation of the following derivatives by standard methods : *amide*, silky needles, m. p. 126°, from light petroleum (Found : C, 71·0; H, 10·0%), less soluble than the *dl-cis*-amide; *anilide*, needles, m. p. 111°, from light petroleum (Found : C, 78·5; H, 8·5%), more soluble than the *dl-cis*-anilide; *p-phenylphenacyl* ester, plates, m. p. 115°, from alcohol (Found : C, 79·4; H, 7·15%); *ethyl* ester (ethyl alcohol–sulphuric acid), b. p. 117—121°/20 mm. (Found : C, 72·6; H, 10·5. $C_{12}H_{20}O_2$ requires C, 73·4; H, 10·3%); *methyl* ester, prepared by means of methyl alcohol–sulphuric acid, b. p. 95°/13 mm., 108°/20 mm., $d_4^{25°}$ 0·9274, $n_D^{25°}$ 1·4614, $[R_L]_D$ 53·97 (calc., 51·99) (Found : C, 72·6; H, 9·7. $C_{11}H_{18}O_2$ requires C, 72·5; H, 9·95%). When the ester was prepared by the action of excess of ethereal diazomethane, the distilled ester contained a crystalline solid, separated by decantation and rinsing with ether. The substance crystallised as needles and decomposed at 128—130° with vigorous evolution of nitrogen; after resolidification the melt had m. p. 100°. The substance was evidently the pyrazoline formed by addition of diazomethane to the double bond of the ester.

Ozonisation. (1) The procedure was exactly that described for the *dl-cis*-acid. *dl-trans*-Caronic acid (520 mg.; 55%) separated rapidly as colourless nodules, m. p. 213°, not depressed by an authentic specimen of the same m. p. prepared by Perkin and Thorpe's method (*loc. cit.*).

(2) The *dl-trans*-methyl ester (4·6 g.) in chloroform (50 c.c.) was treated with excess of ozone at 0°, the solvent removed at room temperature in a vacuum, and the ozonide decomposed by warming on the steam-bath with water (50 c.c.). Excess of solid sodium bicarbonate was added, and the alkaline solution extracted with ether. The aqueous layer was acidified; the solid acid separating (2·33 g.; 53%) crystallised from light petroleum to give *monomethyl* dl-trans-*caronate* as fine plates, m. p. 101—102·5° (Found : C, 55·65; H, 6·8; equiv., by titration, 171·0. $C_8H_{12}O_4$ requires C, 55·8; H, 7·0%; equiv., 172·2). The identity of this half-ester was established by addition of a second equivalent of alkali and warming on the steam-bath until saponification had occurred. Upon acidification and concentration to a small bulk *dl-trans*-caronic acid separated as prisms, m. p. 213°, not depressed by an authentic specimen. Evaporation of the neutral ethereal extract gave, after crystallisation of the volatile solid from light petroleum, bimolecular acetone peroxide, m. p. 132—133° (Found : C, 48·3; H, 8·2. Calc. for $C_6H_{12}O_4$: C, 48·6; H, 8·2%) (Baeyer and Villiger, *Ber.*, 1899, **32**, 3632, record 132—133°).

(3) The *dl-trans*-ethyl ester (4·7 g.), treated with ozone as in (2), gave *monoethyl* dl-trans-*caronate* (2·25 g.; 50%), crystallising from light petroleum in plates, m. p. 73° (Found : C, 57·9; H, 7·7. $C_9H_{14}O_4$ requires C, 58·0; H, 7·6%).

Resolution of the dl-trans-*Acid.*—Attempts to prepare alkaloidal salts with cinchonine, strychnine, and brucine resulted in the separation of the alkaloids. Quinine, cinchonidine, and *l*-α-phenylethylamine salts crystallised from alcoholic solution, though all three salts were very soluble. Fractional crystallisation of the *l*-α-phenylethylamine salt yielded fractions differing only slightly in specific rotation ($[\alpha]_D$ − 7·98° and − 7·10°), and the acid recovered from these fractions was inactive. The cinchonidine and the quinine salt gave evidence of resolution, in both cases the *l-trans*-acid salt separating as the less soluble fraction. Quinine was selected for the resolution.

(1) Quinine (16·2 g.; 0·05 mol.) in alcohol (30 c.c.) was added to the *dl-trans*-acid (8·4 g.; 0·05 mol.) in alcohol (30 c.c.). After 8 hours the first fraction (6·5 g.) was removed, $[\alpha]_D$ − 114·8° (*c*, 1·028). Addition of water (50 c.c.) to the warm mother-liquor gave the second fraction (14·05 g.) after 24 hours, $[\alpha]_D$ −111·6° (*c*, 1·032). A further addition of water (30 c.c.) to the warm mother-liquor gave a third fraction (2·15 g.), $[\alpha]_D$ − 109·7° (*c*, 1·016). The final fraction did not crystallise satisfactorily and the acid recovered from it was only slightly lævorotatory.

Two crystallisations of the first fraction from aqueous alcohol (1 : 1) gave the optically pure *quinine* salt of the *l-trans*-acid (4·4 g.), m. p. 159—161·5°, $[\alpha]_D$ − 115·3° (*c*, 1·023) (Found : C, 72·85; H, 7·9. $C_{10}H_{16}O_2,C_{20}H_{24}O_2N_2$ requires C, 73·1; H, 8·2%). Decomposition of this salt with dilute hydrochloric acid and extraction with ether gave, after evaporation and heating in a vacuum to 80° to remove traces of solvent, *l-trans*-2 : 2-dimethyl-3-*iso*butenyl*cyclo*propane-1-carboxylic acid (1·3 g.) as a viscous oil, $[\alpha]_D$ − 14·01° (*c*, 1·535). After chilling to − 80° and then warming to 0°, the acid crystallised in elongated prisms, m. p. 17—21°, though a trace of crystalline material lingered until 30°.

The natural *d-trans*-acid (chrysanthemum monocarboxylic acid) had $[\alpha]_D$ +14·16° (*c*, 1·554) (Staudinger and Ruzicka, *loc. cit.*, give α_D + 20·1°. No rotations in solution have been recorded). At 0°, on introduction of a crystal of the *l-trans*-acid, the natural acid, previously only known as a liquid, crystallised in elongated prisms, m. p. 17—21°.

The *quinine* salt of the natural *d-trans*-acid had m. p. 97—110°, $[\alpha]_D$ − 109·3° (*c*, 1·010) (Found: C, 70·4; H, 8·15. $C_{10}H_{16}O_2,C_{20}H_{24}O_2N_2,H_2O$ requires C, 70·55; H, 8·3%).

Purification of the intermediate fractions of quinine salt was extremely slow, but a further fraction (1·5 g.) of the quinine salt of the *l-trans*-acid was obtained. The quinine salt of the *d-trans*-acid could not be obtained pure. Acid recovered from salt of the lowest rotation had $[\alpha]_D$ + 7·97° (*c*, 1·550). This acid (0·84 g.) was converted into the *p*-phenylphenacyl ester and fractionally crystallised from light petroleum. The first fraction (1·05 g.), m. p. 115°, consisted of the *dl-trans*-ester. The second fraction was purified by several crystallisations from light petroleum to give the *p*-phenylphenacyl ester of the *d*-trans-acid (0·1 g.), m. p. 66—67°, $[\alpha]_D$ + 32·33° (*c*, 0·402) (Found: C, 79·3; H, 7·0. Calc. for $C_{24}H_{20}O_3$: C, 79·5; H, 7·2%). The *p*-phenylphenacyl ester prepared from the natural *d-trans*-acid had m. p. 66—67°, undepressed on admixture with the above ester, $[\alpha]_D$ + 32·20° (*c*, 1·020) (Haller and La Forge, *J. Org. Chem.*, 1936, **1**, 50, give m. p. 65°).

(2) In another resolution, quinine (32·4 g.; 0·10 mol.) in alcohol (50 c.c.) was added to *dl-trans*-acid (16·9 g.; 0·10 mol.) in alcohol (30 c.c.). After standing overnight, the first fraction (16·7 g.) of salt was removed, $[\alpha]_D$ − 113·6° (*c*, 1·017). Two crystallisations of this fraction from alcohol–water (3 : 2) gave the quinine salt of the *l-trans*-acid (12·1 g.), m. p. 159·5—161°, $[\alpha]_D$ − 115·4° (*c*, 1·014). The *l-trans*-acid (4·0 g.) recovered from this salt had $[\alpha]_D$ − 14·07° (*c*, 1·920). Again it proved impossible to isolate the pure quinine salt of the *d-trans*-acid from the more soluble fractions of this resolution.

The *l-trans*-acid was characterised by the preparation of the following derivatives by standard methods (all crystallisations from light petroleum): *amide*, needles, m. p. 122°, which solidified and remelted at 131—132°, $[\alpha]_D$ − 11·09° (*c*, 0·361) (Found: C, 71·55; H, 9·9. $C_{10}H_{17}ON$ requires C, 71·8; H, 10·2%). The *d-trans*-amide made from the natural acid had m. p. 122°, which solidified and remelted at 131—132° (Staudinger and Ruzicka, *loc. cit.*, give m. p. 131°), $[\alpha]_D$ + 10·65° (*c*, 0·510) (Found: C, 71·8; H, 9·9%). The *dl-trans*-amide was prepared by recrystallising a mixture of 20 mg. of each of the active amides. It melted at 126—127°, alone or mixed with an authentic specimen.

Anilide, m. p. 101°, $[\alpha]_D$ + 2·60° (*c*, 1·540) (note the reversal of sign) (Found: C, 79·4; H, 8·6. $C_{16}H_{21}ON$ requires C, 79·0; H, 8·7%). The *d-trans*-anilide made from the natural acid had m. p. 101° (Staudinger and Ruzicka, *loc. cit.*, give m. p. 101°), $[\alpha]_D$ −2·60° (*c*, 1·540) (Found: C, 79·7; H, 8·6%). 30 Mg. of each of the above anilides were mixed and crystallised. The *dl-trans*-anilide had m. p. 111—112°, alone or mixed with an authentic specimen.

p-*Phenylphenacyl ester*, m. p. 66—67°, $[\alpha]_D$ − 32·11° (*c*, 1·012) (Found: C, 79·3; H, 7·0. $C_{24}H_{20}O_3$ requires C, 79·5; H, 7·2%). 30 Mg. of the *d-trans-p*-phenylphenacyl ester and the above ester were mixed and crystallised. The *dl-trans-p*-phenylphenacyl ester had m. p. 115°, alone or mixed with an authentic specimen.

The authors are indebted to the Advisory Research Council of the Chemical Society and to Imperial Chemical Industries, Ltd., for grants which have covered the costs of chemicals and microanalyses respectively; to Dr. J. C. Smith for suggestions as to the preparation of $\beta\epsilon$-dimethyl-$\Delta^{\alpha\epsilon}$-hexadiene; and to Dr. T. F. West for the gift of a specimen of natural chrysanthemum monocarboxylic acid.

UNIVERSITY COLLEGE, SOUTHAMPTON. [*Received, January 1st*, 1945.]

75. *Catalytic Hydrogenation of Pyrene.*

By J. M. L. CAMERON, J. W. COOK, and WALTER GRAHAM.

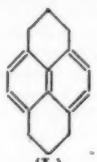
Conditions have been determined for the catalytic hydrogenation of pyrene to hexa-, deca-, and hexadeca-hydrides. *s*-Hexahydropyrene has been converted into the *ketone* (VII).

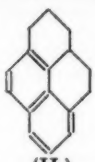
THE increasing availability of the tetracyclic aromatic hydrocarbon, pyrene (see *Ann. Reports*, 1942, **39**, 157), and the development of its chemistry (Vollmann *et al.*, *Annalen*, 1937, **531**, 1) make this hydrocarbon a useful starting point for many synthetic projects. For such a purpose we have sought a convenient process for the preparation of *s*-hexahydropyrene (I), which was prepared by Cook and Hewett (J., 1933, 398) by Goldschmiedt's method (*Annalen*, 1907, **351**, 226) by reduction of pyrene with sodium and amyl alcohol. They obtained *s*-hexahydropyrene in 25% yield, and *as*-hexahydropyrene (II) in 7·5% yield by this process, these yields being increased to 27% and 22%, respectively, by Coulson (J., 1937, 1298), who also studied the hydrogenation of pyrene over a molybdenum–sulphur–active charcoal catalyst. Coulson found pyrene to be rather resistant to hydrogenation, and this accords with the experience of Kaghira (*Bull. Chem. Soc. Japan*, 1931, **6**, 251), who stated that hydrogenation of pyrene with a nickel catalyst was more difficult than that of other hydrocarbons, but claimed a theoretical yield of hexahydropyrene by hydrogenation at 300° for 52 hours.

We have found that pyrene is very readily hydrogenated under suitable conditions. With Raney nickel in *cyclo*hexane at 100° and 130 atm., it was completely hydrogenated to a liquid mixture of hexadecahydropyrenes (III) in 6 hours. When the temperature of hydrogenation was increased to 150—160°, the composition of the mixture was altered and the liquid product deposited crystals of the pure *hexadecahydropyrene* (III), m. p. 90°. Hydrogenation of pyrene with Raney nickel in ethanol at 150° and 160 atm. led to a mixture of decahydropyrenes, from which was obtained a stereochemically pure constituent, m. p. 128° (IV or V). When hydrogenation was carried out in ethanolic solution with copper chromite at 100—110° and 125 atm., it proceeded to the stage of hexahydride, both isomerides (I and II) being isolated. In a series of 7 experiments the yield of the *s*-hexahydride (I) varied between 35% and 45% (average, 40%) and the yield of *as*-hexahydride between 8% and 28% (average, 11%). This is the most satisfactory method yet found for the preparation of *s*-hexahydropyrene, and with more efficient methods of separation of the isomerides the yields would undoubtedly be considerably higher. Samples of pyrene which resisted hydrogenation on account of the presence of catalyst poison were readily susceptible to hydrogenation with a new batch of catalyst.

The ease with which pyrene is completely hydrogenated is of interest in view of the difficulty of hydrogenating the last double bond of phenanthrene (Durland and Adkins, *J. Amer. Chem. Soc.*, 1938, **60**, 1501) and chrysene

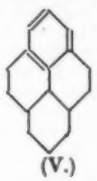
(v. Braun and Irmisch, *Ber.*, 1932, **65**, 883; Spilker, *Angew. Chem.*, 1935, **48**, 368). Although the perhydrides of condensed-ring aromatic hydrocarbons are sometimes resistant to dehydrogenation (Cook, McGinnis, and


(I.)


(II.)

(III.)

(IV.)


(V.)

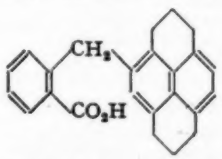
and Mitchell, J., 1944, 286), the perhydropyrene (III), m. p. 90°, was smoothly dehydrogenated to pyrene by palladium-black at 300° in 1½ hours.

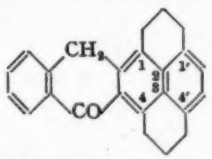
The *decahydropyrene*, m. p. 128°, is different from the three decahydropyrenes previously described (v. Braun and Rath, *Ber.*, 1928, **61**, 956; Coulson, *loc. cit.*). An attempt was made to distinguish between the two possible structures (IV and V) by oxidation of the hydrocarbon with dilute nitric acid, followed by esterification of the acid product. From the mixture of esters was isolated a small amount of a compound, m. p. 110°. The quantity was insufficient for exhaustive purification, but the analytical figures were in good agreement with those for *methyl 5-nitrohemimellitate*. The isomeric 4-nitro-ester has m. p. 144° (Cook and Hewett, J., 1934, 371). This structure has not been confirmed by independent synthesis, but if it is correct the decahydropyrene must be represented by formula (V).

Hydrogenation of anthracene with copper chromite at 100° gave 9 : 10-dihydroanthracene in 90% yield. This procedure is more convenient than the older method of reduction with sodium and amyl alcohol. When the hydrogenation was carried out at 150°, a considerable proportion of the anthracene was converted into *s*-octahydroanthracene.

Condensation of *s*-hexahydropyrene (I) with phthalic anhydride by means of anhydrous aluminium chloride proceeded normally to give a phthaloylic *acid*, which gave only amorphous brown substance that could not be purified when dehydration to a quinone was attempted by benzoyl chloride in boiling α-chloronaphthalene (compare Vollmann, *et al.*, *loc. cit.*) or by boiling benzoyl chloride containing a trace of sulphuric acid (Waldmann, *J. pr. Chem.*, 1938, **150**, 121). The phthaloylic acid was reduced by prolonged treatment with zinc dust and boiling alkali to 1-(o-*carboxybenzyl*)-s-*hexahydropyrene* (VI), which was dehydrated by acetic acid and acetic anhydride containing zinc chloride to 1 : 1′-4 : 4′-*bis*(*trimethylene*)-2 : 3-*benz*-10-*anthrone* (VII).

(VI.)





(VII.)

The formation of the anthrone rather than the anthranyl acetate under these conditions is noteworthy (compare Fieser and Hershberg, *J. Amer. Chem. Soc.*, 1937, **59**, 1032) and illustrates the known reluctance of a dihydronaphthacene structure to pass into a naphthacene structure (Fieser, *ibid.*, 1931, **53**, 2329). The anthrone (VII) showed no tendency whatever to enolise, even with alcoholic potash, and gave no acetate with acetic anhydride in pyridine at 100°. It was recovered unchanged from an attempt to condense it with phenylmagnesium bromide (in boiling ether and in boiling benzene), and also after attempted reduction by the Clemmensen–Martin method (48 hours) and by Clar's zinc-dust fusion method (*Ber.*, 1939, **72**, 1645). In view of the inertness of this ketone its investigation was not pursued.

Experimental.

Hexahydropyrenes.—A suspension of pyrene (35 g.) and Adkins's copper chromite catalyst (8 g.) in ethanol (500 c.c.) was heated with hydrogen in a steel autoclave at 100—105° for 6 hours, with continuous agitation. The initial pressure was 130 atm. The autoclave was opened, and its contents heated to boiling and filtered from catalyst. On cooling, the solution deposited colourless needles of *s*-hexahydropyrene (I) (13 g.), m. p. 132—134°. Concentration of the mother-liquors gave two further crops of crystals, m. p. 90—93° (11 g.) and 93—97° (8 g.). These two fractions were treated separately with picric acid in ethanol, and by fractional crystallisation there were obtained a further quantity (3·1 g.) of *s*-hexahydropyrene and the picrate of *as*-hexahydropyrene (compare Cook and Hewett, *loc. cit.*). This picrate, on treatment with sodium carbonate, gave pure *as*-hexahydropyrene (II) (3·8 g.), m. p. 105°. In other experiments the yields of the two isomerides varied somewhat (see above).

Decahydropyrenes.—A suspension of pyrene (15 g.) and Raney nickel (8 g.) in ethanol (250 c.c.) was heated and stirred with hydrogen under pressure at 150° for 6½ hours. The initial pressure was 160 atm. The filtered solution was distilled under reduced pressure, and gave a colourless liquid (15 g.), b. p. 185—187°/14 mm. After a week in the refrigerator the small amount of crystals which had separated was collected and recrystallised twice from ethanol. This solid *decahydropyrene* (V) formed long, colourless needles, m. p. 127—129° (Found : C, 90·3; H, 9·3. $C_{16}H_{26}$ requires C, 90·5; H, 9·5%). The liquid mixture of decahydropyrenes from which these crystals had separated was redistilled, and had b. p. 183—185°/13 mm. (Found : C, 90·3; H, 9·7%). For oxidation, the crystalline hydrocarbon (0·25 g.) was heated in a sealed tube at 175—180° for 6 hours with concentrated nitric acid (2·5 c.c.) and water (5 c.c.). After cooling, the solution was diluted with water and filtered, and the filtrate evaporated to dryness. The crystalline residue was dissolved in dilute aqueous ammonia, the excess of which was removed by boiling, and the solution was treated with aqueous silver nitrate. The precipitated silver salts (0·35 g.) were dried and their suspension in benzene (4 c.c.) and methyl iodide

(1 c.c.) was boiled for 12 hours. Evaporation of the filtered solution gave a viscous liquid which became crystalline in methanol. Repeated crystallisation from methanol (charcoal) gave tufts of colourless needles, m. p. 110—111°, consisting of *methyl 5-nitrohemimellitate* (Found: C, 48·2; H, 3·5; N, 4·7. $C_{12}H_{11}O_6N$ requires C, 48·5; H, 3·7; N, 4·6%). A fraction from the liquors had m. p. 99—100°, strongly depressed by admixture with methyl hemimellitate, m. p. 102°.

Hexadecahydropyrenes.—(*a*) Pyrene (25 g.) in *cyclo*hexane (150 c.c.) was hydrogenated with Raney nickel (10 g.) at 100° for 6½ hours (initial press., 135 atm.). The product was a colourless liquid, b. p. 171—173°/12 mm. (26 g.) (Found: C, 88·3; H, 11·75. $C_{16}H_{26}$ requires C, 88·0; H, 12·0%). (*b*) In another hydrogenation carried out at 150—160° for 5 hours (initial press., 145 atm.) the product was a liquid, b. p. 315—324°, which partly crystallised. The crystals were drained, and recrystallised from alcohol (1·6 g. from 25 g. of pyrene). The m. p. was 90—91°. This substance did not absorb hydrogen when its ethanolic solution was shaken with hydrogen and Adams's platinum catalyst. For purification, its solution in hexane was shaken with concentrated sulphuric acid. *Hexadecahydropyrene* (III), recovered from the washed hexane solution, separated from ethanol in small, colourless, prismatic needles, m. p. 90—91° (Found: C, 88·15, 87·9; H, 12·0, 11·9. $C_{16}H_{26}$ requires C, 88·0; H, 12·0%).

9 : 10-*Dihydroanthracene.*—Anthracene (25 g.) in ethanol (250 c.c.) was hydrogenated over copper chromite (5 g.) at 100° for 6 hours (initial press., 160 atm.). The resulting 9 : 10-dihydroanthracene (22·5 g.) crystallised in colourless needles, m. p. 109—110°.

1-(*o-Carboxybenzoyl*)-*s-hexahydropyrene.*—Powdered anhydrous aluminium chloride (7·5 g.) was added gradually to a stirred mixture of *s*-hexahydropyrene (10 g.), phthalic anhydride (7·5 g.), and benzene (60 c.c.). Stirring was continued at room temperature for 6 hours, the product decomposed with ice and hydrochloric acid, and the benzene removed in steam. The solid in suspension was collected, extracted with hot dilute sodium carbonate solution, and the extract filtered from unreacted hexahydropyrene (5·1 g.). Acidification of the filtrate precipitated 1-(*o-carboxybenzoyl*)-*s-hexahydropyrene* (8·7 g.), which crystallised from benzene (charcoal) in almost colourless needles, m. p. 176·5—178° (Found: C, 81·0; H, 5·5. $C_{24}H_{20}O_3$ requires C, 80·9; H, 5·6%). Treatment with concentrated sulphuric acid at 65° led to sulphonation.

1-(*o-Carboxybenzyl*)-*s-hexahydropyrene* (VI).—A solution of the keto-acid (2·4 g.) in water (25 c.c.) containing sodium hydroxide (2 g.) was boiled under reflux for 44 hours with zinc dust (5 g.) activated with copper (much lactone was obtained if the period of boiling was curtailed). The filtered solution was acidified with hydrochloric acid and the suspension was boiled for a few minutes to ensure lactonisation of some hydroxy-acid. The reduced *acid* (VI), extracted from the precipitate by sodium carbonate solution and reprecipitated by hydrochloric acid, formed fine colourless needles (2·1 g.) (from benzene), m. p. 215—216° (Found: C, 84·3; H, 6·5. $C_{24}H_{22}O_2$ requires C, 84·2; H, 6·4%).

1 : 1′-4 : 4′-*Bis*(*trimethylene*)-2 : 3-*benz*-10-*anthrone* (VII).—The foregoing acid (1·3 g.) was heated for an hour in an oil-bath at 140—150° with acetic anhydride (5·5 c.c.), acetic acid (10 c.c.), and zinc chloride (0·1 g.). The orange crystals which separated on cooling were collected and washed with ethanol. The *ketone* (VII) (1·1 g.) formed fine orange needles (from benzene–ethanol), m. p. 167—168° (Found: C, 89·1; H, 6·2. $C_{24}H_{20}O$ requires C, 88·9; H, 6·2%). The colour of an alcoholic solution was not deepened by addition of alkali (compare Fieser, *loc. cit.*) and there was no indication of salt formation. Oxidation with sodium dichromate in boiling acetic acid gave an amorphous brown solid which could not be crystallised.

Our thanks are due to the Carnegie Trust of the Universities of Scotland for the award of a Scholarship (to W. G.) and also for a grant for the purchase of an autoclave in which the hydrogenation experiments were performed. We are also indebted to Imperial Chemical Industries Ltd. (Dyestuffs Division) for a gift of pyrene.

UNIVERSITY OF GLASGOW. [*Received, December 28th*, 1944.]

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76. *Polycyclic Aromatic Hydrocarbons. Part XXX. Synthesis of Chrysenols.*

By J. W. COOK and (MISS) R. SCHOENTAL.

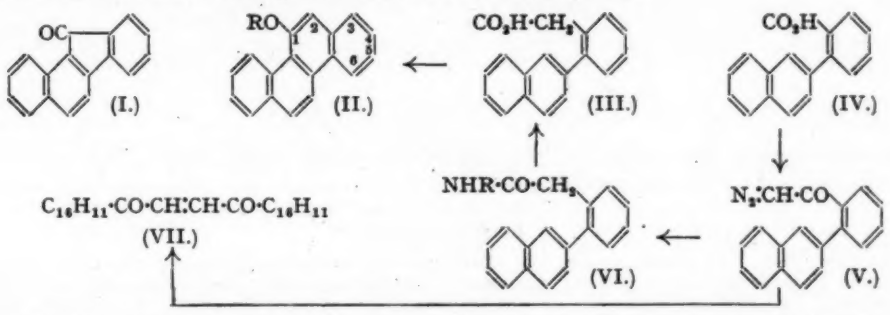
Four new monohydroxychrysenes have been synthesised, so that all six possible isomerides are now known. The *diazo-ketone* formed from α-chrysenic acid (IV) was used for the synthesis of 1-*chrysenol* (II), and was also found to undergo cyclisation to 2-chrysenol under the influence of sulphuric acid in acetic acid. The Reformatsky reaction between the readily accessible methyl γ-bromocrotonate and 1-keto-1 : 2 : 3 : 4-tetrahydrophenanthrene has enabled 3-*chrysenol* to be conveniently synthesised, and 4-*chrysenol* was prepared by modification of the Pschorr phenanthrene synthesis. 6-*Chrysenol* was obtained by dehydrogenation of the known 6-keto-3 : 4 : 5 : 6-tetrahydrochrysene (X).

WHEN polycyclic aromatic hydrocarbons are introduced into the animal body (mice, rats, rabbits) by various routes (orally or by subcutaneous or intraperitoneal injection), they become hydroxylated and eliminated. Evidence has been adduced that the compound so formed in rats and mice from the carcinogenic hydrocarbon, 3 : 4-benzpyrene, is a monohydroxy-derivative (Chalmers and Crowfoot, *Biochem. J.*, 1941, **35**, 1270), probably the 8-hydroxy-compound (Berenblum *et al.*, *Cancer Res.*, 1943, **3**, 151). As part of a systematic study of the metabolism of polycyclic aromatic hydrocarbons, one of us (R. S.) is engaged, in collaboration with Dr. I. Berenblum, in an investigation of the biochemical oxidation of chrysene. To facilitate identification of the products, and also because some monomethoxy-derivatives of polycyclic aromatic hydrocarbons strongly inhibit the growth of tumours (20th *Annual Report of the British Empire Cancer Campaign*, 1943, 20), it was decided to prepare all the six monohydroxychrysenes which are theoretically possible. Two of these have been described previously, and the other four have now been synthesised, together with their methyl ethers.

Ring-enlargement of cyclic ketones by means of diazomethane has been applied to fluorenone by Schultz, Schultz, and Cochran (*J. Amer. Chem. Soc.*, 1940, **62**, 2902), who obtained 9-methoxyphenanthrene as the principal product. By this reaction 1 : 2-benzfluorenone (" chrysene ketone," I) might conceivably have been converted into 1-methoxychrysene (II; R = Me). Although ring-enlargement did take place with diazomethane, most of the ketone (I) did not react, and the only pure product isolated was the known 2-methoxychrysene (Newman and Cathcart, *J. Org. Chem.*, 1940, **5**, 618). 1-*Chrysenol* (II; R = H) was, however, obtained, as its *acetate*, by zinc chloride–acetic anhydride dehydration of 2-(2′-*naphthyl*)*phenylacetic*

acid (III), which was prepared from α-chrysenic acid (IV) by the Arndt–Eistert reaction. α-Chrysenic acid is formed by fusion of 1 : 2-chrysaquinone with alkali and lead dioxide, and the structure (IV) assigned to it by Graebe and Hönigsberger (*Annalen*, 1900, **311**, 257) has been confirmed by Hey and Lawton (J., 1940, 380).

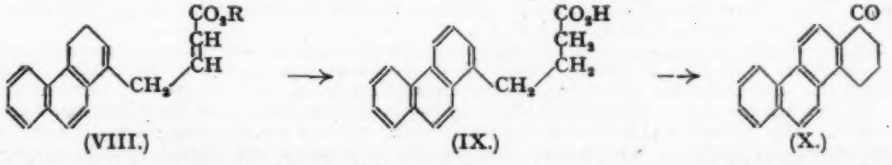
The conditions for the preparation of the chloride of α-chrysenic acid were somewhat critical, as it passed very easily into 1 : 2-benzfluorenone (I). 2-(2′-ω-*Diazoacetyl*)*phenylnaphthalene* (V), obtained by the action of diazomethane on the chloride of (IV), was converted in the normal way into the *amide* (VI; R = H) of the homo-acid (III). This amide was cyclised by sulphuric acid in boiling acetic anhydride to 1-*acetamidochrysene*, oxidised by sodium dichromate in boiling acetic acid to 1 : 2-chrysaquinone.



Addition of the diazo-ketone (V) to a 10% solution of sulphuric acid in acetic acid led to the elimination of nitrogen with formation of 2-chrysenol. This type of cyclisation by decomposition of a diazo-ketone has not hitherto been observed. Possibly the chrysenol is formed directly by rearrangement of the free radical formed by loss of nitrogen, or there may be formed as an intermediate the hydroxymethyl ketone or an ester of this (compare Langenbeck and Baehren, *Ber.*, 1936, **69**, 514; Eistert, *ibid.*, p. 1074). The diazo-ketone (V) was also decomposed with evolution of nitrogen when it was heated with methanol. Analysis of the crystalline *product* suggested that it had structure (VII), formed by union of two bivalent carbon radicals.

Mosettig and Duvall (*J. Amer. Chem. Soc.*, 1937, **59**, 367) found a very satisfactory method for the preparation of 1- and 4-phenanthrols in the action of palladium-black, in a suitable boiling inert solvent, on the corresponding 1- and 4-keto-1 : 2 : 3 : 4-tetrahydrophenanthrenes. This same type of method has been used for the preparation of 5-chrysenol from a 5-ketohexahydrochrysene (Wilds and Shunk, *ibid.*, 1943, **65**, 469), and we have extended it to the preparation of 3- and 6-*chrysenols* by palladium dehydrogenation of the known 3- and 6-keto-3 : 4 : 5 : 6-tetrahydrochrysenes. The 6-keto-compound was prepared by Fieser and Johnson's method (*ibid.*, 1939, **61**, 1647), but an improved method was worked out for 3-keto-3 : 4 : 5 : 6-tetrahydrochrysene (X), as the existing methods of Hoch (*Compt. rend.*, 1938, **207**, 921) and Bachmann and Struve (*J. Org. Chem.*, 1940, **5**, 423) are cumbersome and involve many stages.

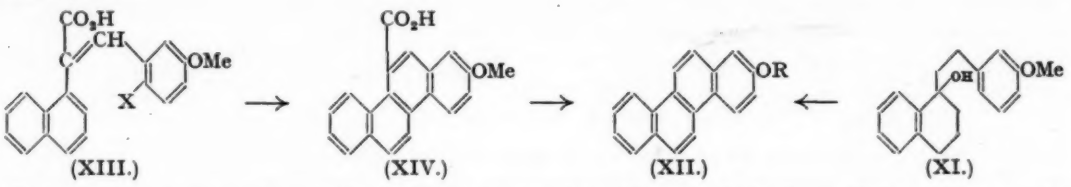
For this new synthesis of (X) advantage was taken of the excellent technique of Ziegler *et al.* (*Annalen*, 1943, **551**, 80) for the preparation of methyl γ-bromocrotonate, and of the significant observation of Ziegler, Schumann, and Winkelmann (*ibid.*, p. 120) that this bromo-ester gives very satisfactory results in the Reformatsky reaction. Methyl γ-bromocrotonate condensed smoothly with zinc and 1-keto-1 : 2 : 3 : 4-tetrahydrophenanthrene to give, after distillation, the unsaturated *ester* (VIII; R = Me). This was isomerised by palladium-black at 280—300° to the methyl ester of γ-1-phenanthrylbutyric acid (IX), which was cyclised by anhydrous hydrogen fluoride (compare Fieser and Hershberg, *J. Amer. Chem. Soc.*, 1939, **61**, 1272) to give the tetracyclic ketone (X) in almost theoretical yield. The final dehydrogenation to 3-chrysenol was effected



by palladium-black in boiling α-methylnaphthalene. This simple procedure for the synthesis of hydroaromatic fused-ring systems has many possible applications, and the method is being further developed in these laboratories.

For the synthesis of 4-*chrysenol* (XII; R = H) two methods have been examined. One of these, based on the work of Cook and Hewett (J., 1933, 1098; 1934, 365) and of Ruzicka and Hösli (*Helv. Chim. Acta*, 1934, **17**, 470), involved the condensation of β-*m*-methoxyphenylethylmagnesium chloride with α-tetralone, followed by dehydration of the crude carbinol (XI) so formed, and then treatment with aluminium chloride in boiling carbon disulphide solution. This gave a mixture of products from which 4-*methoxychrysene* (XII; R = Me) was isolated in very small yield. By-products of the Grignard condensation were 1 : 1′-dihydroxy-1 : 2 : 3 : 4 : 1′ : 2′ : 3′ : 4′-octahydro-1 : 1′-dinaphthyl and its dehydration product 3 : 4 : 3′ : 4′-tetrahydro-1 : 1′-dinaphthyl, the former arising from the reducing action of the Grignard solution on α-tetralone (com-

pare Schroeter, *Ber.*, 1925, **58**, 716; Barnett and Lawrence, J., 1935, 1107). A much more satisfactory method of synthesis of 4-chrysenol was found in a suitable adaptation of the Pschorr phenanthrene synthesis (compare Weitzenböck and Lieb, *Monatsh.*, 1912, **33**, 549). To this end, sodium 1-naphthylacetate was condensed with 2-nitro-5-methoxybenzaldehyde to give a *nitro-acid* (XIII; X = NO_2), which was reduced to the *amino-acid* (XIII; X = NH_2). The diazo-compound prepared from this was cyclised to *4-methoxychrysene-1-carboxylic acid* (XIV) and this was decarboxylated to 4-methoxychrysene, from which 4-chrysenol was obtained by demethylation.



(XIII.) (XIV.) (XII.) (XI.)

All six chrysenols were characterised by the preparation oftheir methyl ethers, their acetates, and their molecular *compounds* with 2 : 7-dinitroanthraquinone.

Experimental.

2-Methoxychrysene from 1 : 2-Benzfluorenone (I).—Ethereal diazomethane, in large excess, was added slowly to a stirred suspension of chrysene ketone (2·3 g.), prepared from chrysaquinone (Bamberger and Burgdorf, *Ber.*, 1890, **23**, 2433), in ether (5 c.c.) and methanol (10 c.c.). After being kept at room temperature overnight, the solution was evaporated, the residue dissolved in light petroleum, and its solution passed through a column of alumina. Five bands were visible in ultra-violet light. The lowest band (colourless, with a violet fluorescence), when eluted with light petroleum and the eluate concentrated, gave crystals of 2-methoxychrysene which, after recrystallisation from benzene–light petroleum, had m. p. 126—127°, alone or mixed with 2-methoxychrysene prepared from chrysene by sulphonation and caustic fusion, with methylation of the chrysenol (U.S.P. 2,032,505; Newman and Cathcart, *loc. cit.*). Identification was completed by preparation from both samples of the same picrate, m. p. and mixed m. p. 165—166°. The molecular *compound* with 2 : 7-dinitroanthraquinone had m. p. 230—231° (from xylene) (Found : C, 71·5; H, 3·9; N, 4·8. $C_{33}H_{20}O_7N_2$ requires C, 71·2; H, 3·6; N, 5·0%).

The yellow band above the colourless band in the chromatogram contained most of the 1 : 2-benzfluorenone unchanged. The coloured bands above this were not examined.

2-(2′-ω-Diazoacetyl)phenylnaphthalene (V).—α-Chrysenic acid (IV) was prepared from 1 : 2-chrysaquinone by the method of Graebe and Hönigsberger (*loc. cit.*) and separated from the more soluble β-chrysenic acid by crystallisation from aqueous acetic acid. It crystallised from benzene in colourless prisms, m. p. 189—190°. For conversion into the chloride, a mixture of the finely powdered α-chrysenic acid (1 g.), pure dry benzene (2 c.c.), and thionyl chloride (2 c.c.) was heated at 40—50° until solution was complete (30—45 mins.). The excess of thionyl chloride and the benzene were removed by evaporation under reduced pressure, and in order to remove the last traces of thionyl chloride the residue was twice evaporated with dry benzene under reduced pressure. If α-chrysenic acid and thionyl chloride were heated together under reflux, or kept at room temperature until solution was complete (several hours), the sole product was 1 : 2-benzfluorenone (I).

A solution of the oily chloride, prepared as described from α-chrysenic acid (1 g.), in pure dry benzene (5 c.c.) was added dropwise to ethereal diazomethane (100 c.c.), prepared from *N*-nitroso-*N*-methylurea (5 g.) (*Organic Syntheses*, 1935, **15**, 3). The solution was kept until evolution of gas ceased (several hours or overnight), and the ether and excess of diazomethane were distilled under slightly reduced pressure. The resulting benzene solution deposited long, pale yellow needles of *2-(2′-ω-diazoacetyl)phenylnaphthalene*, m. p. 131—131·5° with gas evolution (Found : C, 79·6; H, 4·6; N, 10·2. $C_{18}H_{12}ON_2$ requires C, 79·4; H, 4·4; N, 10·3%).

Transformations of 2-(2′-ω-Diazoacetyl)phenylnaphthalene (V).—(*a*) When the solid diazo-ketone was added at room temperature to a 10% solution of concentrated sulphuric acid in acetic acid, gas and heat were liberated, and on pouring the solution into water 2-chrysenol was precipitated; it was identified by direct comparison with an authentic sample. If the acetic acid used as solvent for this reaction was replaced by acetic anhydride, the product was 2-acetoxychrysene (Newman, *J. Amer. Chem. Soc.*, 1938, **60**, 2949).

(*b*) When a suspension of the diazo-ketone in methanol was heated on the water-bath, solution took place with evolution of gas. The *product* formed long, almost colourless needles (probably VII), m. p. 245° (decomp.) (Found : C, 88·2; H, 4·9. $C_{16}H_{14}O_2$ requires C, 88·4; H, 4·9%).

(*c*) When 20% aqueous ammonia was used for attempted conversion of the diazo-ketone into the amide of the homo-acid, as in the examples of Walker (J., 1940, 1304), the diazo-ketone was recovered unchanged. With more dilute ammonia solution the rearrangement was satisfactorily accomplished. A 10% solution of ammonia (20 c.c.) and a 10% solution of silver nitrate (3 c.c.) were added to a solution in dioxan (50 c.c.) of the crude diazo-ketone (from 3 g. of α-chrysenic acid). The mixture was heated on the water-bath, and in a few minutes gas was evolved and the yellow solution became brown and opaque. After ½ hour's heating the hot solution was filtered, and the amide which crystallised on cooling was purified by passing its solution in benzene through a short column of alumina. *2-(2′-Naphthyl)-phenylacetamide* (VI; R = H) formed white needles (1·7 g.) (from benzene), m. p. 162—163° (Found : C, 82·6; H, 5·7; N, 5·4. $C_{18}H_{15}ON$ requires C, 82·8; H, 5·7; N, 5·4%). Hydrolysis with boiling methanolic potash (50 c.c. of 55% aqueous potash and 50 c.c. of methanol) for 4—5 hours gave *2-(2′-naphthyl)phenylacetic acid* (III) (1·6 g.), which crystallised from aqueous methanol in colourless needles, m. p. 123—124° (Found : C, 82·3; H, 5·3. $C_{18}H_{14}O_2$ requires C, 82·4; H, 5·3%).

1-Acetamidochrysene.—A solution of the amide (VI; R = H) in 20% sulphuric acid in acetic anhydride was boiled for 2 hours, and the product purified by chromatographic adsorption on alumina. A fluorescent compound, obtained in small yield, was found to be *1-acetamidochrysene*. It formed fine, colourless needles (from benzene–light petroleum), m. p. 249—250° (Found : C, 84·4; H, 5·3; N, 5·0. $C_{20}H_{15}ON$ requires C, 84·2; H, 5·3; N, 4·9%), and was oxidised by sodium dichromate in boiling acetic acid (1 hour) to 1 : 2-chrysaquinone, m. p. 232—234° (after chromatographic purification), identified by direct comparison with a specimen prepared from chrysene (Graebe and Hönigsberger, *loc. cit.*, p. 262). From another experiment, in which the amide was treated with 20% sulphuric acid in acetic anhydride at room temperature overnight and then at 60° for an hour, there was isolated, in addition to acetamidochrysene, the *acetyl-amide*

(VI; R = Ac). This formed colourless, rhombic crystals (from methanol), m. p. 122—123° (Found: C, 79·2; H, 5·8; N, 4·3. $C_{20}H_{17}O_2N$ requires C, 79·3; H, 5·65; N, 4·6%).

A fruitless attempt was made to convert 1-acetamidochrysene into 1-chrysenol by heating it in a sealed tube with 10% sulphuric acid (6 hours at 215—225° or 19 hours at 200—210°). 2-Aminochrysene was hydrolysed in this way to 2-chrysenol by Newman and Cathcart (*loc. cit.*).

1-*Chrysenol* (II; R = H).—A solution of 2-(2′-naphthyl)phenylacetic acid (100 mg.) in acetic acid (1 c.c.) and acetic anhydride (1 c.c.) together with a trace of zinc chloride was boiled under reflux for an hour (compare Fieser and Hershberg, *J. Amer. Chem. Soc.*, 1937, **59**, 1028; Newman, *ibid.*, 1938, **60**, 2950). The cooled solution was poured into water, giving a resinous precipitate which soon solidified. After being dried, this was separated by fractional crystallisation from light petroleum into the more soluble 1-*acetoxychrysene*, which formed colourless needles (from methanol), m. p. 147—148° (Found: C, 83·7; H, 4·8. $C_{20}H_{14}O_2$ requires C, 83·9; H, 4·9%), and a smaller amount of a less soluble *compound*, which crystallised from benzene in colourless rods, m. p. 209—211° (with evolution of gas). This compound, which was obtained consistently by this cyclisation, may be 1-*acetoxy*-2-*acetylchrysene*, formed from the 1-acetate by a Fries rearrangement with reacetylation of the hydroxy-ketone (Found: C, 80·3; H, 4·7. $C_{22}H_{16}O_3$ requires C, 80·45; H, 4·9%). Its m. p. was greatly depressed by admixture with 1-chrysenol, and it dissolved in alcoholic alkali to give a yellow solution which remained clear on dilution.

Hydrolysis of the crude 1-acetoxychrysene by brief boiling with methanolic potash, followed by distillation of the methanol and acidification of the diluted concentrate, gave 1-*chrysenol* (II; R = H), which, after sublimation in a high vacuum and crystallisation from light petroleum, formed colourless needles, m. p. 208—209° (in an evacuated sealed tube), which became coloured on standing in air (Found: C, 88·35; H, 5·3. $C_{18}H_{12}O$ requires C, 88·5; H, 4·9%). Oxidation with sodium dichromate in boiling acetic acid, gave 1 : 2-chrysaquinone, m. p. 235—236°. The *methyl ether*, prepared from the phenol by 6 hours' boiling with excess of methyl iodide and sodium methoxide in methanol, formed long colourless needles (from benzene–light petroleum), m. p. 142—143° (Found: C, 88·1; H, 5·5; OMe, 12·7. $C_{19}H_{14}O$ requires C, 88·4; H, 5·4; OMe, 12·0%). The *complex* of 1-methoxychrysene with 2 : 7-dinitroanthraquinone (prepared in xylene) formed long, thin, crimson rods, m. p. 220—221° (Found: C, 71·1; H, 3·7. $C_{33}H_{20}O_7N_2$ requires C, 71·2; H, 3·6%). The *benzoate* of 1-chrysenol, prepared with benzoyl chloride and aqueous alkali, formed colourless needles (from light petroleum), m. p. 171—172° (Found: C, 86·0; H, 4·6. $C_{25}H_{16}O_2$ requires C, 86·2; H, 4·6%).

1 : 2-*Diacetoxychrysene*.—This was obtained by 2 hours' boiling with zinc dust of a solution of 1 : 2-chrysaquinone (0·75 g.) in pyridine (10 c.c.) and acetic anhydride (2 c.c.). It formed colourless crystals (from benzene), m. p. 193—194° (Found: C, 76·6; H, 4·6. $C_{22}H_{16}O_4$ requires C, 76·7; H, 4·7%). The compound, m. p. 225—228°, prepared by Knesch (D.R.-P., 151,981) and regarded by him as 1 : 2-diacetoxychrysene must therefore have some other structure. 1 : 2-*Dimethoxychrysene*, prepared by reductive methylation of chrysaquinone, had m. p. 129—130° (Found: C, 83·1; H, 5·4. $C_{20}H_{16}O_2$ requires C, 83·3; H, 5·6%).

5-*Chrysenol*.—This was prepared by the method of Wilds and Shunk (*loc. cit.*) except that the dehydrogenation of the ketohexahydrochrysene with palladium was carried out in boiling α-methylnaphthalene. The chrysenol was formed in good yield in 20 hours, whereas Wilds and Shunk found that 3 days were required in boiling xylene. The *complex* of 5-methoxychrysene with 2 : 7-dinitroanthraquinone had m. p. 268—270° (from xylene) (Found: C, 71·4; H, 3·7. $C_{33}H_{20}O_7N_2$ requires C, 71·2; H, 3·6%).

6-*Chrysenol*.—A solution of 6-keto-3 : 4 : 5 : 6-tetrahydrochrysene (Fieser and Johnson, *loc. cit.*) (1 g.) in mesitylene (10 c.c.) was boiled with palladium-black (0·1 g.) for 20 hours. The filtered solution deposited, on cooling, cream-coloured rosettes of 6-*chrysenol* (0·8 g.) which, after sublimation at 140°/0·2 mm. and crystallisation from benzene–light petroleum, formed almost colourless crystals, m. p. 152—153° (Found: C, 88·4; H, 5·1. $C_{18}H_{12}O$ requires C, 88·5; H, 4·9%). Its *methyl ether*, prepared as described for the 1-isomeride, formed short, cream-coloured needles (from methanol), m. p. 102—103° (Found: C, 88·4; H, 5·6; OMe, 12·5. $C_{19}H_{14}O$ requires C, 88·4; H, 5·4; OMe, 12·0%), and gave a *complex* with 2 : 7-dinitroanthraquinone as orange-red crystals, m. p. 232—234° (Found: C, 71·3; H, 3·6. $C_{33}H_{20}O_7N_2$ requires C, 71·2; H, 3·6%). 6-*Acetoxychrysene*, prepared from the phenol by refluxing with acetic anhydride and pyridine, was sublimed in a vacuum; it then crystallised from light petroleum in colourless needles, m. p. 155—156° (Found: C, 84·1; H, 5·1. $C_{20}H_{14}O_2$ requires C, 83·9; H, 4·9%).

γ-1-(3 : 4-*Dihydrophenanthryl*)*crotonic acid* (VIII; R = H).—Zinc wool (10 g.) was amalgamated by heating with a little dry mercuric chloride in pure dry benzene (40 c.c.) (Hoch, *Bull. Soc. chim.*, 1938, **5**, 274). While the mixture was still warm, 1-keto-1 : 2 : 3 : 4-tetrahydrophenanthrene (Haworth, J., 1932, 1125) (14·9 g.) and methyl γ-bromocrotonate (Ziegler *et al.*, *loc. cit.*) (22·4 g.) were added. Reaction set in immediately, and proceeded without external heat. When its violence had subsided, the whole was heated on the water-bath for ½ hour, and then decomposed with ice and hydrochloric acid. Ether and more benzene were added, and the extract was washed with sodium carbonate solution and water, and dried (sodium sulphate). The solvents were evaporated off, and the residue distilled at 1 mm. The first fraction, to 220°, was largely unreacted ketone (6·5 g.). The main fraction had b. p. about 240° (10 g.) and was a yellow, viscous oil consisting chiefly of the ester (VIII; R = Me). The *acid* (VIII; R = H), obtained by hydrolysis with alcoholic potash, formed yellowish plates (from benzene), m. p. 237—239° (decomp.), and its solution in chloroform decolorised bromine immediately (Found: C, 81·65; H, 6·1. $C_{18}H_{16}O_2$ requires C, 81·8; H, 6·1%). The *methyl* ester, obtained from the pure acid by means of ethereal diazomethane, crystallised from light petroleum in rosettes of almost colourless needles, m. p. 97—98° (Found: C, 82·2; H, 6·8. $C_{19}H_{18}O_2$ requires C, 82·0; H, 6·5%).

γ-1-*Phenanthrylbutyric acid* (IX).—(*a*) The foregoing crystalline ester (200 mg.) was heated with palladium-black (20 mg.) for an hour at 250—280° in an atmosphere of carbon dioxide. The product, which did not crystallise, was hydrolysed with alcoholic alkali. The resulting acid, after purification, had m. p. 152—154° and was identical with that described in the next paragraph.

(*b*) The crude distilled ester from the Reformatsky reaction (8 g.) was heated at 280—300° for 3 hours with palladium-black (0·25 g.) in an atmosphere of carbon dioxide. The acid (6·6 g.) obtained by hydrolysis of the product with alcoholic alkali was recrystallised from alcohol, sublimed at 0·2 mm., and finally crystallised from benzene. The resulting γ-1-phenanthrylbutyric acid had m. p. 155—156° (Bachmann and Struve, *loc. cit.*, give 154·5—155·5°) (Found: C, 81·9; H, 6·1. Calc. for $C_{18}H_{16}O_2$: C, 81·8; H, 6·1%).

3-*Keto*-3 : 4 : 5 : 6-*tetrahydrochrysene* (X).—The acid (IX) (2 g.) was added to anhydrous hydrogen fluoride (20 c.c.) in a platinum crucible which was kept covered for 3—4 hours with occasional stirring. The hydrogen fluoride was then allowed to evaporate, and the residual solid was washed with dilute sodium carbonate solution and dried. The ketone (X) (1·9 g.) was sublimed in a vacuum and recrystallised from benzene, forming colourless leaflets, m. p. 227—228° (Bachmann and Struve give 228—229°) (Found: C, 87·65; H, 5·8. Calc. for $C_{18}H_{14}O$: C, 87·8; H, 5·7%).

3-*Chrysenol*.—Dehydrogenation of the ketone (X) (0·75 g.) by palladium-black (80 mg.) in boiling α-methylnaphthalene (nitrogen atmosphere) to 3-chrysenol (0·55 g.) was complete in 30 hours. When mesitylene was used as the solvent, only a trace of the phenol was obtained in 60 hours. This chrysenol, sublimed at 170—190°/0·2 mm. and recrystallised from benzene, formed colourless leaflets, m. p. 281—283° (in an evacuated sealed tube) (Found: C, 88·3; H, 5·0. $C_{18}H_{12}O$ requires C, 88·5; H, 4·9%). Its *methyl ether*, prepared by 6 hours' boiling with methyl iodide and sodium

methoxide in methanol, formed colourless, lustrous leaflets (from benzene–light petroleum), m. p. 167—168° (Found: C, 88·5; H, 5·35; OMe, 12·5. $C_{19}H_{14}O$ requires C, 88·4; H, 5·4; OMe, 12·0%), and gave a *complex* with 2 : 7-dinitroanthraquinone, m. p. 283—284·5° (from xylene) (Found: C, 71·2; H, 3·6. $C_{33}H_{20}O_7N_2$ requires C, 71·2; H, 3·6%). 3-*Acetoxychrysene*, prepared from the phenol and acetic anhydride in pyridine (2 hours at 100°), formed colourless needles (from benzene), m. p. 235—236° (Found: C, 83·8; H, 5·1. $C_{20}H_{14}O_2$ requires C, 83·9; H, 4·9%).

Condensation of α-Tetralone with β-m-Methoxyphenylethylmagnesium Chloride.—*β-m*-Methoxyphenylethyl alcohol (from *m*-bromoanisylmagnesium bromide and ethylene oxide; Shoesmith and Connor, J., 1927, 2333) was converted into the chloride by treatment with dimethylaniline and thionyl chloride (compare Cook and Hewett, J., 1933, 1107). The Grignard solution prepared from this chloride (17 g.), magnesium turnings (3 g.), activated with iodine, and anhydrous ether (85 c.c.) was treated at 0° with α-tetralone (17 g.) in dry ether (20 c.c.). After being kept overnight, the mixture was worked up in the usual manner, and the product distilled. After removal of lower-boiling material (unchanged chloride and tetralone) a solution of the residual oil in ether was set aside overnight and deposited a small amount of 1 : 1′-dihydroxy-1 : 2 : 3 : 4 : 1′ : 2′ : 3′ : 4′-octahydro-1 : 1′-dinaphthyl, which formed colourless prisms, m. p. 191·5—192·5°, alone or in admixture with a specimen prepared by reduction of α-tetralone by Weidlich's procedure (*Ber.*, 1938, **71**, 1206; compare Schroeter, *loc. cit.*, and Barnett and Lawrence, *loc. cit.*) (Found: C, 81·6; H, 7·3. Calc. for $C_{20}H_{22}O_2$: C, 81·6; H, 7·5%). The ethereal solution from which this diol had been separated was distilled, the principal fraction, which did not crystallise, having b. p. 175—185°/0·5 mm. (10 g.). The highest-boiling fraction (b. p. 200°/0·5 mm.) gave crystals of 3 : 4 : 3′ : 4′-tetrahydro-1 : 1′-dinaphthyl, which had m. p. 140—141° (from ethanol), alone or mixed with an authentic specimen (Found: C, 92·6; H, 7·1. Calc. for $C_{20}H_{18}$: C, 93·0; H, 7·0%).

Dehydration and Cyclisation of the Carbinol (XI).—A mixture of the crude liquid carbinol fraction, b. p. 175—185°/0·5 mm. (see preceding paragraph), and potassium hydrogen sulphate (2 parts) was heated at 170° for an hour, and the product distilled (b. p. 160—170°/0·5 mm.). A mixture of this (2·5 g.) with anhydrous aluminium chloride (2·5 g.) and carbon disulphide (25 c.c.) was heated on the water-bath for 3 hours. After decomposition with ice and hydrochloric acid and washing with dilute sodium hydroxide solution, the solvent was removed, and the residue, dissolved in benzene–light petroleum, was adsorbed on a column of alumina. A colourless fluorescent lower band was eluted with benzene and gave crystals of 4-methoxychrysene, m. p. 245—247°, of which the complex with 2 : 7-dinitroanthraquinone had m. p. *ca.* 250° (see below). More of this methoxy-compound was obtained by methylating with methyl sulphate the alkaline washings referred to above, but the total amount was only a few mg. and the method was not investigated further.

2-*Nitro-5-methoxy-α-1′-naphthylcinnamic Acid* (XIII; X = NO_2).—A mixture of sodium 1-naphthylacetate (20·8 g.) (obtained crystalline by addition of sodium ethoxide to an ethanolic solution of the acid), 2-nitro-5-methoxybenzaldehyde (Mason, J., 1925, **127**, 1195) (18·1 g.), zinc chloride (2 g.), and acetic anhydride (180 g.) was heated in an oil-bath at 120—130° for 4 hours. The acetic anhydride was decomposed with water. The reddish, resinous material which separated was triturated with ether, which left undissolved a pink solid (20·4 g.). This, after several crystallisations from toluene–ethanol (charcoal), gave cream-coloured, rhombic crystals of the *nitro-acid* (XIII; X = NO_2), m. p. 218·5—219·5° (Found: C, 68·9; H, 4·4; N, 4·3. $C_{20}H_{15}O_5N$ requires C, 68·8; H, 4·3; N, 4·0%). The ethereal extract of the crude acid was mixed with ethanol; the solution then slowly deposited crystals which, after recrystallisation from alcohol, formed dark red needles, m. p. 160—161° (Found: C, 75·6; H, 4·3; N, 5·2%). The structure of this *compound*, which was insoluble in sodium carbonate solution, has not been investigated.

2-*Amino-5-methoxy-α-1′-naphthylcinnamic Acid* (XIII; X = NH_2).—A 40% solution of ferrous sulphate (250 c.c.) was added to a solution of the nitro-acid (10 g.) in 15% aqueous ammonia (250 c.c.), the mixture heated for 2 hours on the water-bath, filtered from iron hydroxides, and the precipitate extracted repeatedly with hot 1% aqueous ammonia. The combined filtrate and extracts were acidified with acetic acid, and the precipitated *amino-acid* (XIII; X = NH_2) (7·5 g.) was recrystallised from ethanol. A sample for analysis was purified through its hydrochloride, m. p. 246—247° (decomp.), which was sparingly soluble in cold water, and then formed colourless needles (from ethanol), m. p. 220—221° (decomp.) (Found: C, 75·6; H, 5·45; N, 4·5. $C_{20}H_{17}O_3N$ requires C, 75·2; H, 5·3; N, 4·4%).

4-*Methoxychrysene-1-carboxylic Acid* (XIV).—A 5% solution of sodium nitrite (17 c.c.) was added to a solution of the amino-acid (XIII; X = NH_2) (5 g.) in 8% sulphuric acid (250 c.c.). The solution was kept overnight at room temperature, during which a voluminous yellowish precipitate separated. This was dissolved by addition of ethanol (250 c.c.), the solution made just alkaline with sodium carbonate (the total volume of solution being 1 l.), and then heated at 50° for 1—2 hours. When reaction was complete, nitrogen evolution ceased and the solution no longer gave a colour with alkaline β-naphthol. The precipitate obtained by acidification was recrystallised from methanol (yield, 1·2 g.) and then several times from benzene and methanol. 4-*Methoxychrysene-1-carboxylic acid* (XIV) formed long, pinkish needles, m. p. 244—245° (Found: C, 79·3; H, 4·5. $C_{20}H_{14}O_3$ requires C, 79·4; H, 4·6%). Its crystalline chloride, prepared by the action of thionyl chloride at 40°, reacted with boiling methanol to give the *methyl* ester, which crystallised from methanol in almost colourless needles, m. p. 172—173° (Found: C, 79·8; H, 5·0; OMe, 19·9. $C_{21}H_{16}O_3$ requires C, 79·7; H, 5·1; OMe, 19·6%).

4-*Methoxychrysene.*—Decarboxylation of the acid (XIV) (1 g.) with copper chromite (0·25 g.) in pure quinoline (14 c.c.) at 230—250° (bath temp.) was complete in 4 hours. A solution of the neutral product in tetrachloroethane was purified by passage through a column of alumina. On concentration, 4-*methoxychrysene* (0·75 g.) crystallised and formed colourless leaflets (from benzene), m. p. 250—251° (Found: C, 88·65; H, 5·5; OMe, 11·8. $C_{19}H_{14}O$ requires C, 88·4; H, 5·4; OMe, 12·0%). Its scarlet *complex* with 2 : 7-dinitroanthraquinone had m. p. 240—241° (from xylene) (Found: C, 71·2; H, 3·7. $C_{33}H_{20}O_7N_2$ requires C, 71·2; H, 3·6%).

4-*Chrysenol.*—A solution of the methoxy-compound (250 mg.) in acetic acid (10 c.c.) and hydrobromic acid (*d*, 1·7; 7 c.c.) was boiled for 2 hours, poured into water, the precipitate dissolved in dilute sodium hydroxide, and the filtered solution acidified. The resulting 4-*chrysenol* was sublimed in a high vacuum and recrystallised from benzene, forming pinkish needles, m. p. 273—275° (in an evacuated sealed tube) (Found: C, 88·4; H, 5·0. $C_{18}H_{12}O$ requires C, 88·5; H, 4·9%). The *acetate*, obtained from this chrysenol by brief boiling with acetic anhydride and a little pyridine, formed almost colourless needles (from benzene), m. p. 229—230° (Found: C, 84·25; H, 4·9. $C_{20}H_{14}O_2$ requires C, 83·9; H, 4·9%).

4-*Methoxy*-1 : 2-*chrysaquinone.*—A solution of the acid (XIV) (0·1 g.) and sodium dichromate (0·6 g.) in acetic acid (7 c.c.) was boiled for an hour and poured into water. The precipitate, dissolved in benzene, was adsorbed on a column of alumina. On developing the chromatogram with benzene there were obtained (*a*) a dark band at the top of the column, (*b*) a red band below this, and (*c*) the least strongly adsorbed band which fluoresced strongly in ultra-violet light. The red band (*b*) was eluted with chloroform, and the chromatography repeated. The material so purified gave deep red, rhombic needles, m. p. 233—234° (from benzene), of 4-*methoxy*-1 : 2-*chrysaquinone* (Found: C, 79·0; H, 4·3. $C_{19}H_{12}O_3$ requires C, 79·2; H, 4·2%).

The band (*c*), when eluted, gave long, yellowish crystals, m. p. 236—238°, which, after sublimation in a high vacuum and crystallisation from benzene, had m. p. 239—240°, depressed strongly by admixture with the red 1 : 2-quinone. Analysis suggested that this was an isomeric *quinone*, possibly 4-methoxy-3 : 6-chrysaquinone, although this structure

does not readily accommodate the fact that decarboxylation had occurred during oxidation (Found: C, 79·3; H, 4·1. $C_{19}H_{12}O_3$ requires C, 79·2; H, 4·2%).

These experiments have been carried out by one of us (R. S.) working on behalf of the Oxford University Centre of the British Empire Cancer Campaign, to whom we express our thanks. All microanalyses were by Mr. J. M. L. Cameron.

UNIVERSITY OF GLASGOW. [*Received, December 28th*, 1944.]

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77. *The Cyclic Methyleneamines. The Use of Hexamine in the Production of Aldehydes.*

By JOHN GRAYMORE and (in part) DAVID R. DAVIES.

Sommelet showed that hexamine–benzyl chloride on hydrolysis gave benzaldehyde. It is now demonstrated that benzylamine and its derivatives can be converted into the corresponding aldehydes by means of hexamine. In a similar manner α-phenylethylamine gives acetophenone.

By hydrolysis of the quaternary compounds which hexamine forms with alkyl halides Hoch (D.R.-P. 139,394) obtained primary amines. Sommelet (*Compt. rend.*, **1913**, **157**, 852) showed that, when boiled with water, the quaternary derivatives broke down to give an aldehyde other than formaldehyde as the main product, hexamine–benzyl chloride yielding 70% of benzaldehyde together with some benzylamine and methylamine. He presumed that methylenebenzylamine, formed by fission of the quaternary compound, isomerised to benzylidenemethylamine, hydrolysis of which would give benzaldehyde.

On this assumption it was obvious that benzaldehyde should be obtainable in good yield from methylenebenzylamine or indeed directly from benzylamine. The authors have found that, when benzylamine is added to formaldehyde an oil is produced which, when just dissolved in hydrochloric acid, reacts with an aqueous solution of hexamine to give benzaldehyde in 60% yield. Similarly, the solution obtained by adding concentrated hydrochloric acid to pure methylenebenzylamine till it just dissolves also gives benzaldehyde when heated with hexamine. No benzaldehyde is obtained from either benzylamine or methylenebenzylamine in absence of hexamine or in presence of an excess of hydrochloric acid.

Ingold (J., **1929**, 1199) observed that methylenebenzylamine exhibits prototropic mobility in presence of sodium hydroxide at 300°. His results, which indicated a 10% conversion into benzylidenemethylamine (based on the yield of benzaldehyde obtained by hydrolysis of the product), are not comparable with those obtained by the use of hexamine in aqueous solution. The low result is probably due to polymerisation of methylenebenzylamine in presence of sodium hydroxide to tribenzyltrimethylenetriamine, whereby isomerisation to benzylidenemethylamine is precluded.

According to Clarke, Gillespie, and Weisshaus (*J. Amer. Chem. Soc.*, **1933**, **55**, 4571) the production of methylamine when certain amino-acids are heated with formaldehyde in acid solution is due, in the first place, to transposition of the double bond in a Schiff's base:

$$CH_2{:}N{\cdot}CHR{\cdot}CO_2H \longrightarrow CH_2{\cdot}N{:}CR{\cdot}CO_2H$$

The results now obtained show that methylenebenzylamine is initially formed as a result of the hydrolysis of hexamine–benzyl chloride. Under conditions unfavourable to the formation of tribenzyltrimethylenetriamine, isomerisation to benzylidenemethylamine ensues. Finally, benzaldehyde is produced by interaction of the benzylidenemethylamine and aminomethyl alcohol (from hexamine):

$$CHPh{:}NMe + H_2O + NH_2{\cdot}CH_2{\cdot}OH \longrightarrow Ph{\cdot}CHO + NHMe{\cdot}CH_2{\cdot}OH + NH_3$$

Ammonia is evolved copiously during hydrolysis of hexamine–benzyl chloride.

o-, *m*-, and *p*-Chlorobenzylamine can be similarly converted into *o*-, *m*-, and *p*-chlorobenzaldehyde, but in considerably lower yields than that obtained from benzylamine.

The method, when extended to α-phenylethylamine gave, as expected, acetophenone.

Distillation under reduced pressure of hexamine–benzyl chloride yielded a colourless oil to which the structure (I) has been assigned. Its behaviour is similar to that of other cyclic triamines; it decomposes

$$\text{(I.)}\quad NMe\begin{<}\begin{matrix}CH_2\text{—}NMe\\ CHPh{\cdot}NMe\end{matrix}\end{>}CHPh + 3H_2O \longrightarrow 2Ph{\cdot}CHO + 3NH_2Me + CH_2O$$

readily on warming with mineral acids to give benzaldehyde, methylamine, and formaldehyde.

EXPERIMENTAL.

Hexamine–p-nitrobenzyl Bromide.—*p*-Nitrobenzyl bromide (1 mol.) was added to hexamine (1 mol.) in chloroform, and the mixture refluxed (2 hrs.). The quaternary *compound* separated in needles, m. p. 168° (decomp.) (Found: Br, 22·4. $C_{13}H_{18}O_2N_5Br$ requires Br, 22·5%).

Hexamine–o-nitrobenzyl iodide, obtained in a similar way, crystallised in deep yellow needles, m. p. 154° (Found: I, 31·7. $C_{12}H_{18}O_2N_5I$ requires I, 31·5%).

Preparation of Benzaldehyde from Benzylamine.—Benzylamine (25 g.) was dissolved in water (25 c.c.), and formaldehyde (25 c.c. of 40%) added with cooling. The sticky oil which separated was dissolved by the addition of concentrated hydrochloric acid (25 c.c.), and the solution heated to its b. p. under reflux. Hexamine (25 g.), dissolved in a small

quantity of warm water, was added, and the whole refluxed (15 mins.). After excess of acid had been added and the solution again refluxed (5 mins.) to decompose any condensation product which the benzaldehyde might have formed, the latter was extracted with ether, dried over calcium chloride, and distilled, b. p. 179° (16 g., 66%).

When only 10 g. of hexamine were used, a considerably smaller yield of the aldehyde was obtained, and from benzylamine (25 g.), water (25 c.c.), formaldehyde (25 c.c. of 40%), and excess of concentrated hydrochloric acid (65 c.c.) together with hexamine (10 g.), no benzaldehyde resulted.

Action of Hexamine on Methylenebenzylamine.—A solution of methylenebenzylamine (10 g.) in concentrated hydrochloric acid (10 c.c.) was heated to its b. p. under reflux, hexamine (10 g.) added, and, after refluxing for 15 mins., the mixture was made acid with excess of hydrochloric acid. The oil which had separated was removed in ether, recovered, and distilled; benzaldehyde (5 g.) was obtained.

Distillation of Hexamine–Benzyl Chloride.—Hexamine–benzyl chloride (30 g.), prepared by heating hexamine with benzyl chloride in chloroform solution, was heated under 30 mm. The mass rapidly charred, ammoniacal vapours were given off, and an oil distilled at 68—75°. On redistillation a colourless oil was obtained, b. p. 70—72°/30 mm. (Found: C, 76·5; H, 8·6; N, 15·1. $C_{18}H_{23}N_3$ requires C, 76·8; H, 8·2; N, 15·0%).

Hydrolysis. After the oil (5 g.) had been refluxed with excess of hydrochloric acid for 10 minutes, the benzaldehyde which had separated was extracted with ether, dried, and distilled, b. p. 179° (phenylhydrazone, m. p. and mixed m. p. 153°) (1·8 g.). The residual liquor after the extraction was evaporated to dryness on the water-bath; formaldehyde was evolved. The residue was dissolved in alcohol (in which it was completely soluble) and evaporated to remove traces of formaldehyde. Addition of sodium hydroxide liberated methylamine, identified by conversion into 2 : 4-dinitrophenylmethylamine, m. p. and mixed m. p. 175°.

Action of Hexamine Hydrochloride on Methylenebenzylamine.—Hexamine hydrochloride (9 g.), precipitated from a chloroform solution of hexamine by dry hydrogen chloride, was intimately mixed with methylenebenzylamine (9 g., prepared by addition of formaldehyde to an aqueous solution of benzylamine, the sticky oil, after repeated washing with water, being dried over concentrated sulphuric acid and crystallised from light petroleum; m. p. 45—46°) and heated under reduced pressure. Considerable charring with evolution of ammoniacal vapours ensued and a small quantity of oil, which on redistillation gave a colourless oil (2 g.), was obtained, b. p. 72°/30 mm. (Found: N, 15·2. $C_{18}H_{23}N_3$ requires N, 15·0%). Hydrolysed with hydrochloric acid, it gave benzaldehyde, methylamine, and formaldehyde.

Hexamine–Chlorobenzyl Chlorides.—*p*-, *o*-, and *m*-Chlorobenzyl chloride with hexamine (1 mol. of each) in hot chloroform gave the corresponding quaternary derivatives, white crystals, m. p. 198° (Found: Cl, 23·7. Calc. for $C_{13}H_{18}N_4Cl_2$: Cl, 23·6%), white solid, m. p. 204—205° (Found: Cl, 23·8%), and white crystals, m. p. 205° (Found: Cl, 23·7%), respectively.

p-*Chlorobenzylamine.*—Hexamine–*p*-chlorobenzyl chloride (50 g.) was dissolved in excess of hydrochloric acid, the solution steam-distilled until evolution of formaldehyde ceased, and the liquor evaporated to 150 c.c. On cooling, *p*-chlorobenzylamine hydrochloride crystallised; recrystallised from aqueous alcohol, it formed needles (22 g.), m. p. 250° (Found: N, 7·9. Calc. for C_7H_8NCl,HCl: N, 7·9%). The base was obtained from it as an oil (13 g.) b. p. 218—224°/775 mm. (Found: N, 9·9. Calc. for C_7H_8NCl: N, 9·9%).

m-Chlorobenzylamine hydrochloride (25 g.), obtained in a similar way from hexamine–*m*-chlorobenzyl chloride (50 g.), crystallised from alcohol in flakes, m. p. 225° (Found: N, 7·9%). The base was obtained as an oil, b. p. 226°/760 mm.

o-Chlorobenzylamine (15 g.) was prepared by decomposition of the corresponding quaternary derivative (35 g.). After evaporation of the residual liquor almost to dryness, the base was liberated by addition of sodium hydroxide, extracted in ether, and distilled; b. p. 220°/775 mm. (Found: N, 9·8%). 2 : 4-*Dinitrophenyl-o-chlorobenzylamine*, obtained from the base and 2 : 4-dinitrochlorobenzene in alcohol, formed yellow needles, m. p. 116—117°, from alcohol (Found: N, 13·6. $C_{13}H_{10}O_4N_3Cl$ requires N, 13·7%).

p-*Chlorobenzaldehyde.*—To *p*-chlorobenzylamine (10 g.) was added formaldehyde (5 c.c. of 40%), followed by sufficient hydrochloric acid (50 : 50) to dissolve the condensation product. The solution was made up to 100 c.c. and brought to the b. p., hexamine (5 g.) added, and the mixture refluxed (15 mins.). An excess of hydrochloric acid was now added, and the mixture boiled for 5 minutes and cooled. The oil, which solidified, was extracted with ether, from which it crystallised, m. p. 45°, yield 5 g. It was identified as *p*-chlorobenzaldehyde by conversion into the 2 : 4-dinitrophenylhydrazone, m. p. 265°.

o-*Chlorobenzaldehyde.*—To *o*-chlorobenzylamine (8 g.) formaldehyde (4 c.c. of 40%) was added. The emulsion formed was just cleared by addition of hydrochloric acid, and the solution diluted to 100 c.c. Addition of hexamine (5 g.), followed by refluxing (½ hr.), resulted in the separation of an oil, which was extracted with ether. From the extract, after washing with hydrochloric acid and drying over calcium chloride, *o*-chlorobenzaldehyde (3 g.) was obtained, b. p. 210—214°; it was identified by conversion into its 2 : 4-dinitrophenylhydrazone, m. p. and mixed m. p. 207°.

m-*Chlorobenzaldehyde.*—By the method described in the preceding case, *m*-chlorobenzylamine (10 g.), formaldehyde (5 c.c. of 40%), and hexamine (10 g.) gave *m*-chlorobenzaldehyde (5 g.), b. p. 212—214°, identified by conversion into its 2 : 4-dinitrophenylhydrazone, m. p. and mixed m. p. 245°.

Acetophenone from α-Phenylethylamine.—Formaldehyde (13 c.c. of 40%) and water (50 c.c.) were added to α-phenylethylamine (20 g.). The emulsion was shaken (15 mins.) to complete the reaction, just cleared by addition of dilute hydrochloric acid, and brought to its b. p. Hexamine (12 g.) was added, and the mixture refluxed (1 hr.). After cooling, the oil which had separated was extracted with ether, washed with dilute hydrochloric acid, dried over calcium chloride, and distilled, b. p. 202°. It was identified as acetophenone. Yield, 6 g.

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78. *Researches in the Phenanthridine Series. Part VI. The Relationship between Structure and Trypanocidal Properties.**

By LESLIE P. WALLS

(with a Note by C. H. BROWNING, K. M. CALVER, and M. W. LECKIE).

Certain amino-substituted quaternary salts of this series possess trypanocidal properties, and the effect of variation in number and position of the substituents has been investigated. An improvement has been effected

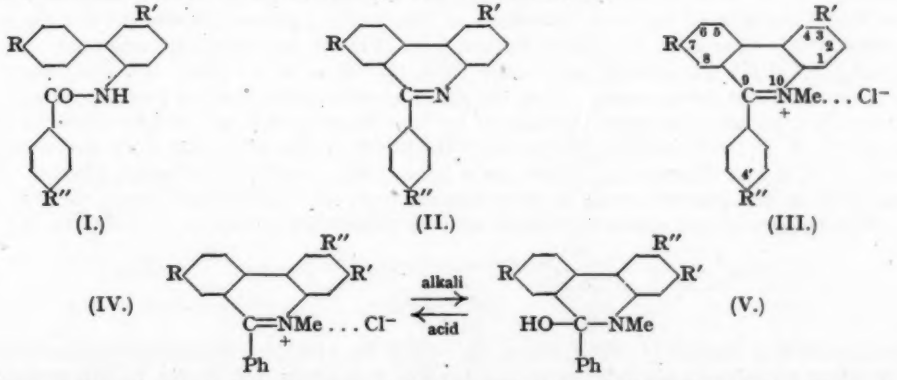
* Much of the work described in this paper forms the subject of B.PP. 511,353 and 520,273 and recent provisional specifications.

in the method of ring closure of acyl-*o*-xenylamines (I→II), and it has been found that the facile preparation of nitro-quaternary salts such as 2 : 7-dinitro-9-phenyl-10-methylphenanthridinium chloride (IV; R = R′ = NO_2, R″ = H), followed by reduction, offers an alternative and generally preferable route to the trypanocidal types. In order to obtain a similar bromo-substituted compound it has been shown that bromination of 4′-nitro-2-acetamidodiphenyl occurs as expected in the 5-position.

Activity against *T. congolense* is well maintained in all the diamino-quaternary salts except when both amino-substituents are in the 9-phenyl group. Pronounced action against *T. brucei* is only found in (IV; R = R′ = NH_2, R″ = H), where the amino-groups are in the " benzidine " position. Acetylation of the amino-groups results always in diminution in activity.

THE discovery that 7-amino-9-*p*-aminophenyl-10-methylphenanthridinium chloride (III; R = R″ = NH_2, R′ = H), referred to as No. 897, exerts a curative action in *T. congolense* infections in mice and cattle (Browning, Morgan, Robb, and Walls, *J. Path. Bact.*, **1938**, **46**, 203; Browning, Browning, and Robb, *ibid.*, 1940, **50**, 371; Hornby, Evans, and Wilde, *J. Comp. Path. Ther.*, **1943**, **53**, 269; Carmichael and Bell, *ibid.*, **1944**, **54**, 49) has led to the investigation of analogous compounds. A valuable improvement in method has resulted from the observation that in the conversion of acyl-*o*-xenylamines, *e.g.*, (I), into the corresponding phenanthridines, *e.g.*, (II), by phosphorus oxychloride, both the rate of condensation and the yield of product are increased by the addition to the reagents of an inert, high-boiling liquid miscible with them. Nitrobenzene answers the purpose well, and its function is simply thermal, in that it permits reaction to be performed at 180—200°. In several of the examples given below the yield of phenanthridine derivative has been increased by this means from a small amount to over 50%.

An alternative route to the desired amino-quaternary salts, *e.g.*, (IV; R = R″ = NH_2, R′ = H), has been found in the facile reduction of the nitro-quaternary salts (compare IV; R = R″ = NO_2, R′ = H), which themselves are readily prepared directly from the nitrophenanthridines. For instance, 3- and 7-amino-9-*p*-aminophenyl-10-methylphenanthridinium chloride, (III; R′ = R″ = NH_2, R = H) and (III; R = R″ = NH_2, R′ = H), described by Morgan and Walls (J., 1938, 389), are both more conveniently prepared by this method, which is shorter than the alternative by two stages, protection of amino-groups by acetylation and subsequent deacetylation. Moreover, a further disadvantage of the older method is evaded : with several of the diaminophenylphenanthridines, notably 2 : 7-*diamino-9-phenylphenanthridine* (see below), the two amino-groups are not severally and quantitatively monoacetylated, and the isolation of the desired compound in which both amino-groups are protected is not readily accomplished. By the addition of alkali to aqueous solutions of the nitro-quaternary salts, crystalline pseudo-bases are precipitated, *e.g.* (V; R = R″ = NO_2, R′ = H), which are reconverted by dissolution in dilute acids into the original salts. These salts are almost colourless, highly crystalline substances of indefinite melting-decomposition point which dissolve in dilute acid, but are subject to partial hydrolysis to pseudo-bases by water alone. Reduction to the corresponding amino-quaternary salts proceeds very smoothly with iron and water, preferably in the absence of acid, but catalytic hydrogenation under pressure generally involves nuclear reduction, a phenomenon which is probably associated with high reactivity of the $>C{:}\overset{+}{N}Me$ grouping.



Modification of the structure of the trypanocidal type (III; R = R″ = NH_2, R′ = H) has been effected in the following ways :

(i) *Elimination of one amino-group.* The compound (III; R″ = NH_2, R = R′ = H) has already been described (Morgan and Walls, J., 1931, 2447) and is devoid of trypanocidal properties. Its isomeride (III; R = NH_2, R′ = R″ = H) has now been prepared by the improved methods.

(ii) *Substitution of the 9-phenyl group with* m-*amino- in place of* p-*amino-.* In view of the promising trypanocidal properties of the compounds (III; R = R″ = NH_2, R′ = H) and (III; R′ = R″ = NHAc, R = H) it was desirable to determine whether a favourable therapeutic effect would follow when the substituent R″ = NH_2 or NHAc was in the *m*-position. The synthesis of these types was readily effected by the new methods.

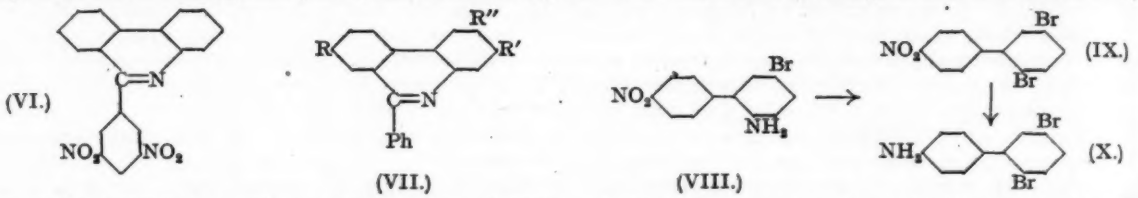
(iii) *Placing of both amino-groups in the 9-phenyl substituent.* 3″ : 5″-Dinitrobenzamidodiphenyl was condensed by phosphorus oxychloride to 9-3′ : 5′-*dinitrophenylphenanthridine* (VI). Methylation of this dinitro-

compound readily afforded the *methochloride*, which was reduced by stannous chloride to **9-3' : 5'-*diamino*-*phenyl*-10-*methylphenanthridinium chloride***. An attempt to prepare this salt by the alternative route involving reduction of (VI) to the diamino-compound and protection of the amino-groups by acetylation before methylation failed owing to lack of reactivity of the diacetamido-compound with the usual methylating agents.

(iv) *Placing of both amino-groups in the phenanthridine part of the molecule.* Isolation of a small yield of 3 : 7-dinitro-9-phenylphenanthridine (VII; R = R'' = NO_2, R' = H) from the ring-closure of 5 : 4'-dinitro-2-benzamidodiphenyl has already been reported (J., 1938, 389). The yield has been increased to over 50% by the use of a phosphorus oxychloride–nitrobenzene mixture. Conversion of the product into the desired quaternary salt (IV; R = R'' = NH_2, R' = H) was effected by the alternative routes: methylation, followed by reduction with iron powder and water; or reduction to 3 : 7-diamino-9-phenylphenanthridine (VII; R = R'' = NH_2, R' = H), protection of the amino-groups by acetylation, and then methylation, followed by hydrolysis to **3 : 7-*diamino*-9-*phenyl*-10-*methylphenanthridinium chloride*** (IV; R = R'' = NH_2, R' = H).

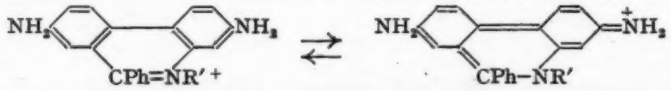
The isomeric type (IV; R = R' = NH_2, R'' = H) was prepared by a similar series of reactions from 4 : 4'-dinitro-2-aminodiphenyl (Finzi and Bellavita, *Gazzetta*, 1938, **68**, 77). The final product, **2 : 7-*diamino*-9-*phenyl*-10-*methylphenanthridinium bromide***, is of particular interest because of its amino-groups being in the " benzidine " position. It was expected to possess enhanced substantive characteristics, which should be reflected in its chemotherapeutic properties. The salt crystallises in almost black prisms, purple by transmitted light. The crystals and their aqueous solution closely resemble permanganate in appearance.

(v) *Introduction of a halogen atom into the active molecule.* The toxicity of several acridine antimalarials and antiseptics is known to be diminished by the introduction of a halogen atom. A representative of this type was obtained as follows. Bromination of 4'-nitro-2-acetamidodiphenyl afforded a monobromo-derivative. Hydrolysis of this compound yielded an amine (VIII), which was converted by Hodgson and Walker's method



(J., 1933, 1620) into a dibromonitro-compound (IX), and the latter by successive reduction and oxidation into respectively the dibromo-amino-compound (X) and 2 : 5-dibromobenzoic acid. Hence, bromination had occurred in the 5-position.* The amine (VIII) was *p*-nitrobenzoylated, and the product (I; R = R'' = NO_2, R' = Br) cyclised to **3-*bromo*-7-*nitro*-9-p-*nitrophenylphenanthridine*** (II; R = R'' = NO_2, R' = Br). Conversion into the desired quaternary salt (III; R = R'' = NH_2, R' = Br) was effected through the diacetamido-derivative (II; R = R'' = NHAc, R' = Br); the alternative route was not satisfactory.

The colour relationships of the salts described in this paper conform generally with those described in Part V (J., 1938, 389); thus salts of amines derived from (VI) are not markedly coloured: those from (VII; R = R'' = NH_2, R' = H) are orange, and those from (II; R = R'' = NH_2, R' = Br) deep red like the corresponding bromine-free compounds. That the diamino-salts referred to in sections (i) and (ii), in which the *p*-amino-group is either missing or is replaced by a *m*-amino-group, are deeply coloured shows that an amino-group in the 3- or the 7-position, particularly the latter, of the phenanthridine molecule has a marked chromophoric effect, a fact difficult to explain on a benzenoid–quinonoid resonance theory. Reference has already been made to the intense colour of salts derived from the " benzidine " type (IV; R = R' = NH_2, R'' = H). Here benzenoid–quinonoid resonance may be postulated (compare J., 1931, 2447):



According to Kumler and Daniels (*J. Amer. Chem. Soc.*, 1943, **65**, 2190), bacteriostatic properties in the sulphonamide and acridine series are associated with this type of resonance, but so far in this series no clear conclusion can be drawn that this type of resonance specificially favours either bacteriostatic or trypanocidal action.

Note on Chemotherapeutic Trypanocidal Action.†

The results of the investigation of these amino-quaternary compounds for trypanocidal action in experimentally infected mice are shown in the table, the methods employed being those to which references are given. Two species of trypanosomes have been used, *viz.*, *T. brucei* and *T. congolense*, one strain of each. The former is allied to the causal agents of African trypanosomiasis of man and behaves similarly towards drugs. The latter affects cattle and other domestic animals in Africa, but not man; its behaviour towards

* Since going to press (VIII) and its acetyl derivative have been described by Case (*J. Amer. Chem. Soc.*, 1945, **67**, 118), and their constitution proved by substantially the same method.

† Work done with the support of the Medical Research Council in the Department of Bacteriology and Pathology, The University and Western Infirmary, Glasgow.

drugs differs strikingly from that of *T. brucei*, since most classes of compounds which are highly active against *T. brucei* have little or no effect on *T. congolense*. It must be noted that in assessing the chemotherapeutic activity of a substance, toxicity for the mammalian host is the limiting factor; hence the largest doses used approach the maximum which the animal will tolerate without serious toxic effects. The most striking features of the present series are as follows. For comparison results obtained under similar conditions with compounds **893**, **894**, and **897** (Nos. 19, 20, and 23 in Morgan and Walls, *loc. cit.*) are given.

(1) All the amino-compounds show distinct trypanocidal action except that in which the amino-substituents are restricted to the 9-phenyl group (1052).

(2) *T. congolense* is more strongly influenced as a rule than *T. brucei*, each infection being treated at the most susceptible stage—*e.g.*, Nos. 1508, 1568, which are the analogues of No. 897 with the amino-group of the 9-phenyl radical in the 3′- instead of the 4′-position; also, 1505 and 1506, 1565 and 1553, and 1573. This is in agreement with our previous findings in the phenanthridine series.

(3) Comparison of the structure of the more effective compounds (894; 1505, 1506; 1508, 1568; 1573; 1565, 1553) indicates that action is obtained with various positions of the amino-groups. The 2 : 7-diamino-compounds (1565, 1553), which possess a " benzidine " type of structure, are the most active against both species of trypanosome.

(4) Acetylation of the two amino-groups in the active substances greatly reduces the therapeutic efficiency even where the solubility is not markedly diminished, cf. Nos. 894, 893; 1508, 1507; 1573, 1574. In the table the orientations of the compounds are denoted as in (III), the Cl^- being replaced by the anion A^-.

		Therapeutic effect in mice infected with *T. congolense* (Strain I).[1]		*T. brucei*.[2]	
Compound.	Formula.	Dose, in mg.(a)	Result.	Dose, in mg.(a)	Result.
897	$NH_2 = 7 : 4', A = Cl$	0·033	Cure	1	(Cure)
		0·01	(Cure)		
896	$NHAc = 7 : 4', A = Cl$	0·5	O	1	O
894	$NH_2 = 3 : 4', A = Cl$	0·2—0·02	Cure	0·2	Slight
		0·01	Slight—O		
893	$NHAc = 3 : 4', A = Cl$	2·5	(Cure)	2·5	Cure
				1·25	Marked
1505	$NH_2 = 7, A = Cl$	0·5—0·1	Cure	0·5	Cure
		0·016	Marked	0·33	Slight
1506	$NH_2 = 7, A = I$	0·33—0·05	Cure	0·33	Marked
		0·016—0·01	Slight		
1504	$NHAc = 7, A = Cl$	10 †	Cure	10	O
		2·5	Marked		
1508	$NH_2 = 7 : 3', A = Cl$	1·6—0·022	Cure	1·6	Cure
		0·01—0·005	(Cure)	0·33	Marked
		0·0033	Slight		
1568	$NH_2 = 7 : 3', A = I$	1·3—0·02	Cure	0·66	(Cure)
		0·01	(Cure)		
1507	$NHAc = 7 : 3', A = Cl$	5	(Cure)	3·3	O
		2·5	Slight		
1573	$NH_2 = 3 : 3', A = Cl$	0·33	Cure	0·5	O
		0·033—0·01	(Cure)		
1574	$NHAc = 3 : 3', A = Cl$	2·5	Slight	2·5	O
1061	$NO_2 = 3' : 5', A = Cl$	0·5	(Cure)	2	O
		0·25	Slight		
1052	$NH_2 = 3' : 5', A = Cl$	0·5	Slight	2	O
1053	$NHAc = 3' : 5', A = Cl$	0·5	Slight	1	O
1542	$NH_2 = 3 : 7, A = Cl$	0·66	Cure	0·33	Cure
		0·01	(Cure)	0·05	Marked
1162	$NHAc = 3·7, A = Cl$	1	O	2	Slight—O
1565	$NH_2 = 2 : 7, A = Cl$	0·33—0·005	Cure	0·33	Cure
		0·0033	(Cure)	0·16—0·05	(Cure)
1553	$NH_2 = 2 : 7, A = Br$	0·33—0·005	Cure	0·33	Cure
		0·0025	Marked	0·1	(Cure)
1554	$NHAc = 2 : 7, A = Cl$	0·5	Slight	0·5	O
1141	$NH_2 = 7 : 4', Br = 3, A = Cl$	0·25—0·05	Cure	1	Slight
		0·02	Slight		
1142	$NHAc = 7 : 4', Br = 3, A = Cl$	0·5	O	2*	O

* Maximum solubility. † Partly undissolved.

(*a*) Dosage is reckoned per 20 g. of body weight, 1 c.c. of solution being injected subcutaneously: the highest dose shown is not less than half the average maximum tolerated.

The terms used to designate degrees of trypanocidal action are as follows:

Cure = Complete sterilisation of infection.
(Cure) = Cure effected only in a proportion of the animals treated.
Marked = Absence of parasites from blood for 10 days or longer.
Slight = Disappearance of parasites from blood for several days.
O = No effect.

[1] See Browning and Calver, *J. Path. Bact.*, 1943, **55**, 393; treatment was given at the acme stage.
[2] See Browning *et al.*, *ibid.*, 1934, **39**, 75; 1938, **46**, 203; the strain of trypanosome used was " Paris III " and treatment was given 24 hours after inoculation.

Experimental.

3-Nitro-9-p-nitrophenyl-10-methylphenanthridinium Methosulphate.—A solution of 3-nitro-9-*p*-nitrophenylphenanthridine (3 g.; J., 1938, 839) in nitrobenzene (30 ml.) was boiled to expel moisture, cooled to 180°, and methyl sulphate (3 g.) added. When the reaction had subsided the solution was boiled for 30 mins. and then distilled in steam. The residual liquor was filtered from a small quantity of unchanged material, and on being cooled deposited the *methosulphate* in high yield in buff-coloured plates of indefinite melting-decomposition point (Found: N, 9·15. $C_{21}H_{17}O_8N_3S$ requires N, 8·9%).

The 7-nitro-methosulphate was similarly prepared and converted into the *methochloride* by heating its aqueous solution with hydrochloric acid; the salt crystallised from water in pale yellow prisms (Found: N, 10·85; Cl, 9·15. $C_{20}H_{14}O_4N_3Cl$ requires N, 10·6; Cl, 9·0%).

Reduction in aqueous solution by iron filings of either of the foregoing salts was rapid. The red filtrate was made just alkaline with ammonia, filtered from a small amount of amorphous material, made just acid with hydrochloric acid, and evaporated to small bulk. On neutralisation, the corresponding diamino-quaternary salt crystallised in high yield.

7-Nitro-9-phenylphenanthridine.—A solution of 4′-nitro-2-aminodiphenyl (20 g.) in hot nitrobenzene (40 ml.) was treated with benzoyl chloride (9 ml.), and boiled gently until evolution of hydrogen chloride ceased. On being cooled, *4′-nitro-2-benzamidodiphenyl* was deposited in high yield; it crystallised from benzene in colourless acicular prisms, m. p. 165·5° (Found: N, 8·85. $C_{19}H_{14}O_3N_2$ requires N, 8·8%). This benzoyl derivative (15 g.), phosphorus oxychloride (30 g.), and nitrobenzene (45 g.) were heated together under reflux at 170—180° for 12 hours. The product was carefully stirred into water, and a complex of *7-nitro-9-phenylphenanthridine* and acid separated from the nitrobenzene. When the complex was heated with aqueous alkali the desired product (14 g.) was liberated; it crystallised from pyridine in fine yellow, silky needles, m. p. 237° (Found: N, 9·4. $C_{19}H_{12}O_2N_2$ requires N, 9·35%). When nitrobenzene was omitted from the reaction mixture, only about a quarter of this yield resulted, most of the diphenyl derivative being recovered unchanged.

This base was converted by the above method into the methosulphate, and addition of hydrochloric acid to its solution precipitated the *methochloride*, which crystallised from boiling water in stout, buff-coloured prisms (Found: N, 8·25; Cl, 9·8. $C_{20}H_{15}O_2N_2Cl$ requires N, 8·0; Cl, 10·1%).

7-Amino-9-phenyl-10-methylphenanthridinium chloride (1505) was obtained by reduction of the foregoing salt with iron powder and water. As before, addition of ammonia to the aqueous solution of the filtrate precipitated a brown amorphous impurity. Evaporation of the slightly acid solution to small bulk afforded the quaternary salt in large brown transparent rhombs, m. p. 235·5° (decomp.) (Found: N, 8·65; Cl, 10·95. $C_{20}H_{17}N_2Cl$ requires N, 8·7; Cl, 11·05%). The *iodide* (1506) crystallised from water in transparent red prisms, m. p. 188—190° (decomp.) (Found: C, 57·9; H, 4·1; N, 7·15; I, 31·0. $C_{20}H_{17}N_2I$ requires C, 58·2; H, 4·1; N, 6·9; I, 30·85%).

On being warmed with acetic anhydride, the chloride was converted into the *acetyl* derivative (1504); it crystallised from a large volume of water in yellow plates, m. p. 275° (decomp.) (Found: C, 73·0; H, 5·4; N, 7·75; Cl, 9·9. $C_{22}H_{19}ON_2Cl$ requires C, 72·85; H, 5·25; N, 7·7; Cl, 9·8%).

7-Nitro-9-m-nitrophenylphenanthridine.—*4′-Nitro-2-m-nitrobenzamidodiphenyl*, prepared from 4′-nitro-2-aminodiphenyl and *m*-nitrobenzoyl chloride in nitrobenzene solution, crystallised from glacial acetic acid in small white needles, m. p. 187° (Found: N, 11·5. $C_{19}H_{13}O_5N_3$ requires N, 11·55%). This compound (25 g.), phosphorus oxychloride (50 g.), and nitrobenzene (75 g.) were heated under reflux from a bath at 180° for 12 hours. On being stirred into water, the desired *product* (19·5 g.) separated directly from the nitrobenzene layer. After filtration it was washed successively with nitrobenzene, water, and hot methylated spirit, and finally crystallised from nitrobenzene or a large volume of pyridine in matted, cream-coloured needles, m. p. 269° (Found: N, 12·45. $C_{19}H_{11}O_4N_3$ requires N, 12·2%). Its *methochloride*, prepared as for similar salts, crystallised from water in transparent, buff-coloured prisms which disintegrated on exposure to air owing to loss of water of crystallisation (Found, for dehydrated salt: N, 10·65; Cl, 8·95. $C_{20}H_{14}O_4N_3Cl$ requires N, 10·6; Cl, 9·0%).

7-Amino-9-m-aminophenyl-10-methylphenanthridinium chloride (1508), obtained from the foregoing salt by reduction with iron and water, crystallised from water in red prisms, m. p. 147—149° (decomp.) (Found: C, 71·2; H, 5·5; N, 12·65; Cl, 10·6. $C_{20}H_{18}N_3Cl$ requires C, 71·5; H, 5·35; N, 12·5; Cl, 10·6%). The *iodide* (1568) crystallised from water in red prisms, m. p. 240° (decomp.) (Found: I, 29·55. $C_{20}H_{18}N_3I$ requires I, 29·75%). The *diacetyl* derivative (1507) crystallised from water in minute yellow prisms, m. p. 237·5° (decomp.) (Found: C, 68·75; H, 5·2; N, 10·25; Cl, 8·55. $C_{24}H_{22}O_2N_3Cl$ requires C, 68·65; H, 5·25; N, 10·0; Cl, 8·45%).

Except where otherwise stated, the following compounds were prepared by similar methods, all in excellent yields.

3-Nitro-9-m-nitrophenylphenanthridine.—*5-Nitro-2-m-nitrobenzamidodiphenyl* formed almost colourless needles from glacial acetic acid, m. p. 190·5° (Found: N, 11·6. $C_{19}H_{13}O_5N_3$ requires N, 11·55%), and the *phenanthridine* almost white, matted needles from nitrobenzene, m. p. 269° (Found: N, 12·5. $C_{19}H_{11}O_4N_3$ requires N, 12·2%). When the latter compound (5 g.) in nitrobenzene solution (30 ml.) was heated with methyl sulphate (3 ml.), the very sparingly soluble methosulphate crystallised almost quantitatively, so steam-distillation was unnecessary. The salt was separated, washed with nitrobenzene and several times with hot benzene. It was then heated in suspension in aqueous ammonia, and the yellow pseudo-base thus liberated was dissolved in N-hydrochloric acid. On being cooled, the solution deposited the rather sparingly soluble *methochloride* in cream-coloured, matted needles, the yield being almost theoretical (Found: N, 10·55; Cl, 8·6. $C_{20}H_{14}O_4N_3Cl$ requires N, 10·6; Cl, 9·0%).

3-Amino-9-m-aminophenyl-10-methylphenanthridinium Chloride (1573).—This *chloride* crystallised from water in golden-yellow needles, m. p. 199—202° (decomp.) (Found: N, 12·45; Cl, 10·4. $C_{20}H_{18}N_3Cl$ requires N, 12·5; Cl, 10·6%). Its *diacetyl* derivative (1574) separated from water as rather ill-defined, pale yellow prisms, m. p. 215—217° (decomp.) (Found: N, 10·2; Cl, 8·2. $C_{24}H_{22}O_2N_3Cl$ requires N, 10·0; Cl, 8·45%).

9-3′: 5′-Dinitrophenylphenanthridine (VI).—*2-3″: 5″-Dinitrobenzamidodiphenyl*, obtained by condensation of excess of *o*-xenylamine with 3 : 5-dinitrobenzoyl chloride in hot pyridine, crystallised from benzene in yellow plates, m. p. 185° (Found: N, 11·7. $C_{19}H_{13}O_5N_3$ requires N, 11·55%), and the *compound* (VI) crystallised from pyridine or nitrobenzene in small, buff prisms, m. p. 294° (Found: N, 12·0. $C_{19}H_{11}O_4N_3$ requires N, 12·2%). Its *methochloride* (1061) crystallised from water in buff, feathery needles (Found: N, 10·8; Cl, 8·65. $C_{20}H_{14}O_4N_3Cl$ requires N, 10·6; Cl, 9·0%).

9-3′: 5′-Diaminophenyl-10-methylphenanthridinium Chloride (1052).—The foregoing salt (4 g.) was well powdered and suspended in alcohol (100 ml.) and concentrated hydrochloric acid (20 ml.). Rapid reduction occurred on addition of stannous chloride (16 g.), dissolution of the nitro-compound being followed by crystallisation of a yellow stannichloride. When the aqueous solution of this salt was partly neutralised stannic hydroxide was precipitated; complete neutralisation caused the *diamino-methochloride* to crystallise in brownish plates (2·5 g.), m. p. 241° (decomp.) (Found: C, 72·2; H, 5·45; N, 12·95; Cl, 10·2. $C_{20}H_{18}N_3Cl$ requires C, 71·55; H, 5·35; N, 12·5; Cl, 10·6%). Its *diacetyl* derivative (1053) crystallised from water as pale yellow prismatic needles, m. p. 227° (decomp.) (Found: C, 68·65; H, 5·1; N, 10·1; Cl, 8·05. $C_{24}H_{22}O_2N_3Cl$ requires C, 68·65; H, 5·25; N, 10·0; Cl, 8·45%).

3 : 7-*Dinitro*-9-*phenylphenanthridine*.—5 : 4′-Dinitro-2-benzamidodiphenyl (23 g.), nitrobenzene (69 ml.), and phosphorus oxychloride (46 g.) were heated in a bath at 180° for 18 hours. The phenanthridine (12·3 g.) separated from the nitrobenzene layer when the product was stirred into water. On steam-distillation of the nitrobenzene mother-liquor a crudely crystalline residue was left which consisted largely of unchanged diphenyl derivative, and from which a further yield of the phenanthridine could be obtained by retreatment with nitrobenzene–phosphorus oxychloride mixture.

3 : 7-*Diamino*-9-*phenylphenanthridine*.—A suspension of the foregoing dinitro-compound in alcoholic hydrochloric acid was reduced by stannous chloride. When the red solution obtained was poured into aqueous sodium hydroxide solution it furnished the *diamino*-compound as a pale yellow crystalline precipitate, very soluble in alcohol; it was best crystallised from benzene, forming clusters of discoloured prisms, m. p. 194° (Found : C, 80·0; H, 5·3; N, 14·6. $C_{19}H_{15}N_3$ requires C, 80·0; H, 5·25; N, 14·7%). Its *diacetyl* derivative crystallised from alcohol in almost colourless prisms, m. p. 266° (Found : C, 74·5; H, 5·25; N, 11·4. $C_{23}H_{19}O_2N_3$ requires C, 74·8; H, 5·15; N, 11·4%).

When this acetyl compound (1 g.) in hot nitrobenzene (25 ml.) was treated with methyl *p*-toluenesulphonate, the solvent removed by steam-distillation, and the residual aqueous liquor treated with sodium chloride, 3 : 7-*diacetamido*-9-*phenyl*-10-*methylphenanthridinium chloride* (1162) crystallised in yellow plates, m. p. 285° (decomp.) (Found : C, 68·8; H, 5·4; N, 10·2; Cl, 8·4. $C_{24}H_{22}O_2N_3Cl$ requires C, 68·65; H, 5·25; N, 10·0; Cl, 8·45%).

3 : 7-*Diamino*-9-*phenyl*-10-*methylphenanthridinium chloride* (1542) was obtained from the diacetyl salt by hydrolysis with concentrated hydrochloric acid. Neutralisation with ammonia liberated the *diamino-chloride* as a brown gum, which slowly crystallised. Recrystallisation from water furnished brown prisms, m. p. 268° (decomp.) (Found : C, 71·8; H, 5·15; N, 12·7; Cl, 10·45. $C_{20}H_{18}N_3Cl$ requires C, 71·55; H, 5·35; N, 12·5; Cl, 10·6%).

3 : 7-*Dinitro*-9-*phenyl*-10-*methylphenanthridinium chloride* crystallised from dilute hydrochloric acid in buff prisms (Found : N, 10·75; Cl, 9·45. $C_{20}H_{14}O_4N_3Cl$ requires N, 10·6; Cl, 9·0%). When its aqueous solution was treated with ammonia, the pseudo-base 3 : 7-*dinitro*-9-*phenyl*-10-*hydroxy*-10-*methyl*-9 : 10-*dihydrophenanthridine* was precipitated. It was sparingly soluble in alcohol or benzene, but crystallised in golden-yellow needles, m. p. 221—223° (decomp.), on addition of hot alcohol to its pyridine solution (Found : N, 11·05. $C_{20}H_{15}O_4N_3$ requires N, 11·15%). The dinitro-quaternary salt was readily reduced to the corresponding diamino-salt by iron filings and water.

2 : 7-*Dinitro*-9-*phenylphenanthridine*.—4 : 4′-*Dinitro*-2-*benzamidodiphenyl*, prepared from 2-amino-4 : 4′-dinitrodiphenyl and benzoyl chloride in hot chlorobenzene, separated from glacial acetic acid solution in almost colourless prisms, m. p. 234° (Found : N, 11·8. $C_{19}H_{13}O_4N_3$ requires N, 11·55%). By the standard procedure it afforded the *phenanthridine* in about 50% yield, unchanged diphenyl compound being recovered; pale yellow needles were obtained by crystallisation from nitrobenzene (Found : N, 12·2. $C_{19}H_{11}O_4N_3$ requires N, 12·2%). Reduction of this compound in alcoholic suspension with stannous chloride–hydrochloric acid, or with hydrogen under pressure using a platinum-black catalyst, furnished the *diamine*, which crystallised from alcohol in golden-yellow prisms, m. p. 198° (Found : C, 79·8; H, 5·45; N, 14·7. $C_{19}H_{15}N_3$ requires C, 80·0; H, 5·25; N, 14·75%).

2 : 7-*Dinitro*-9-*phenyl*-10-*methylphenanthridinium chloride* crystallised from water in buff-coloured prisms (Found : N, 10·7; Cl, 8·65. $C_{20}H_{14}O_4N_3Cl$ requires N, 10·6; Cl, 8·95%). The *pseudo-base* crystallised from acetone in small red prisms, m. p. 186—188° (decomp.) (Found : N, 10·9. $C_{20}H_{15}O_4N_3$ requires, N, 11·15%).

2 : 7-*Diamino*-9-*phenyl*-10-*methylphenanthridinium Bromide* (1553).—The permanganate-like solution from the reduction of the foregoing dinitro-quaternary salt (20 g.) with iron filings and water was diluted to *ca.* 600 ml., treated with potassium bromide (6 g.), and made just alkaline with ammonia. It was then purified chromatographically from a purple-black by-product by filtration through a column (8 cm. long by 4 cm. diam.) of talc. The filtrate was neutralised, and concentrated under reduced pressure to 200 ml. On being cooled, the *bromide* crystallised in purple-black, elongated plates (first crop 15 g.), m. p. 241—243° (decomp.) (Found : C, 62·8; H, 4·95; N, 11·35. $C_{20}H_{18}N_3Br$ requires C, 63·15; H, 4·75; N, 11·05%). When the solution was chromatographed without addition of potassium bromide, and the filtrate evaporated to dryness under reduced pressure a purple-black gum was obtained, and on being boiled with alcohol this rapidly afforded purple-black plates of the *chloride* (1565), decomp. *ca.* 253° (Found : Cl, 10·45. $C_{20}H_{18}N_3Cl$ requires Cl, 10·6%). This salt was extremely soluble in water, and boiling acetic anhydride rapidly converted it into the *diacetamido-chloride* (1554); aqueous solutions of this compound were liable to set to a jelly, but from aqueous alcohol (1 : 1) minute yellow needles separated, m. p. 260° (decomp.) (Found : N, 9·9; Cl, 8·5. $C_{24}H_{22}O_2N_3Cl$ requires N, 10·0; Cl, 8·45%).

5-*Bromo*-4′-*nitro*-2-*acetamidodiphenyl*.—A solution of 4′-nitro-2-acetamidodiphenyl (21 g.) in glacial acetic acid (210 ml.) was added with stirring to a solution of bromine (14·7 g.) in the same solvent (147 ml.). After 24 hours the solid product was collected; it recrystallised from glacial acetic acid in small yellow prisms (23·5 g.), m. p. 214° (Found : N, 8·55; Br, 23·5. $C_{14}H_{11}O_3N_2Br$ requires N, 8·4; Br, 23·9%). This *acetyl* compound was refluxed for 6 hours with alcoholic hydrochloric acid (1 : 1), the hydrochloride separated, and decomposed with alkali, yielding the *amine* (VIII), which crystallised from alcohol in orange-red, acicular prisms, m. p. 152° (Found : N, 9·45; Br, 27·0. $C_{12}H_9O_2N_2Br$ requires N, 9·55; Br, 27·3%). Hodgson and Walker's modification of the Sandmeyer reaction converted this amine into 2 : 5-*dibromo*-4′-*nitrodiphenyl* (IX), which crystallised from alcohol in almost colourless prisms, m. p. 98° (Found : N, 4·25; Br, 44·2. $C_{12}H_7O_2NBr_2$ requires N, 3·9; Br, 44·8%).

2 : 5-*Dibromo*-4′-*aminodiphenyl* (X), obtained quantitatively from the nitro-compound by reduction with iron and acidified water, crystallised from alcohol in light brown prisms, m. p. 95° (Found : N, 4·5. $C_{12}H_9NBr_2$ requires N, 4·3%). It was oxidised slowly by alkaline permanganate, and the only product isolated was 2 : 5-dibromobenzoic acid, m. p. 156°, alone or in admixture with an authentic specimen (cf. Claus and Weil, *Annalen*, 1892, **269**, 223).

5-*Bromo*-4′-*nitro*-2-p-*nitrobenzamidodiphenyl* crystallised from nitrobenzene in pale yellow prisms, m. p. 245° (Found : N, 9·6; Br, 18·0. $C_{19}H_{13}O_5N_3Br$ requires N, 9·5; Br, 18·1%).

3-*Bromo*-7-*nitro*-9-p-*nitrophenylphenanthridine* was obtained in high yield by the nitrobenzene–phosphorus oxychloride method; pale yellow needles from nitrobenzene, m. p. 348° (Found : N, 10·15; Br, 18·5. $C_{19}H_{10}O_4N_3Br$ requires N, 9·9; Br, 18·85%). Catalytic reduction of this compound with hydrogen caused removal of the bromine atom, so the following method was used : the well-powdered compound (5 g.) was suspended in 40 ml. of a glacial acetic acid solution of stannous chloride saturated with hydrogen chloride (compare Thiele and Dimroth, *Annalen*, 1899, **305**, 114). After 24 hours the red salt that had separated was removed and converted into the 7-*amino*-compound, which crystallised from pyridine–benzene in yellow prisms, m. p. 265° (Found : C, 62·9; H, 3·95; N, 12·1; Br, 22·0. $C_{19}H_{14}N_3Br$ requires, C, 62·65; H, 3·85; N, 11·55; Br, 22·05%). The *diacetyl* compound crystallised from alcohol in hard, colourless, solvated cubes, or from nitrobenzene in clusters of white microscopic needles, m. p. 301° (Found : C, 62·0; H, 4·0; N, 9·45; Br, 17·6. $C_{23}H_{18}O_2N_3Br$ requires C, 61·6; H, 4·0; N, 9·35; Br, 17·85%).

3-*Bromo*-7-*amino*-9-p-*aminophenyl*-10-*methylphenanthridinium Chloride* (1141).—Although methyl sulphate caused profound decomposition of 3-bromo-7-acetamido-9-*p*-acetamidophenylphenanthridine in hot nitrobenzene, yet with methyl *p*-toluenesulphonate smooth condensation took place. After steam-distillation of the solvent, the crude residue was hydrolysed with hydrochloric acid, and on neutralisation the diamino-quaternary *chloride* crystallised in transparent red prisms, m. p. 265° (decomp.), which were purified by recrystallisation from water (Found : C, 57·75; H, 3·75; N, 10·4; Cl, 8·35. $C_{20}H_{17}N_3ClBr$ requires C, 57·9; H, 4·1; N, 10·15; Cl 8·55%). The *diacetyl* compound (1142

crystallised from a large volume of alcohol in solvated, pale yellow, matted needles, m. p. 213° (decomp.). After removal of solvent the salt rapidly absorbed 4 mols. of water from the atmosphere (Found, for hydrated salt: C, 50·7; H, 5·15; Cl, 5·9; Br, 13·3; loss on heating, 12·35. $C_{24}H_{21}O_2N_3ClBr,4H_2O$ requires C, 50·5; H, 5·1; Cl, 6·2; Br, 14·0; H_2O, 12·6%).

Most of the quaternary salts described above are hydrated, the degree of hydration often depending on the humidity of the atmosphere. Consequently, analyses refer to the dried salts unless otherwise stated.

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79. *The Determination of Small Amounts of Aluminium in Spelter.*

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The aluminium content of spelter has an important bearing on its behaviour in hot-dip galvanising. Existing methods for the separation and determination of small amounts of aluminium have been improved and adapted to the analysis of spelter.

IN the modern "hot-dip" galvanising process, aluminium is added to the galvanising bath in order to improve the appearance, uniformity, and flexibility of the coating. At the same time, the thickness of the coating may be decreased, depending on the amount of aluminium added.

A rigid control of the aluminium contents of the bath—ranging from 0·01 to 0·1%—has to be maintained, so an accurate and rapid method of determination is required. The bath made up from spelter according to B.S.S. 222 should contain not more than 1·25% of lead, 0·07% of iron, 0·02% of tin, 0·02% of antimony and arsenic, and 0·25% of cadmium, the remainder being zinc.

The separation of aluminium from large amounts of zinc by ammonia is troublesome and unsatisfactory. The elimination of interfering elements can be achieved with the help of a mercury cathode cell (Scherrer and Mogerman, *J. Res. Nat. Bur. Stand.*, 1938, **21**, 106) but necessitates special equipment, and the complete removal of zinc from a larger sample of spelter takes several hours.

Kolthoff and Stenger and their co-workers (*J. Amer. Chem. Soc.*, 1934, **56**, 812; *Ind. Eng. Chem. Anal.*, 1942, **14**, 797) introduced ammonium benzoate as an analytical reagent which separates aluminium from zinc, cadmium, and iron(II), but small amounts of zinc are co-precipitated. With the help of this reagent, a method has been adopted, based on the following separations. Lead and tin remain undissolved when the sample is treated with a dilute sulphuric–hydrochloric acid mixture in the presence of excess of zinc. Aluminium, together with iron(III), is precipitated as benzoate and subsequently freed from iron and co-precipitated zinc by treatment with hydrogen sulphide in ammoniacal tartrate solution (Haslam, *Analyst*, 1933, **58**, 270). Aluminium is finally precipitated as the 8-hydroxyquinoline derivative and estimated volumetrically.

EXPERIMENTAL.

Special Solutions.—(i) Ammonium acetate, 500 g./l. (ii) Ammonium benzoate, 100 g./l., with addition of 1 mg. of thymol. (iii) Ammonium benzoate wash-liquid: 100 ml. of reagent (ii) diluted to 1 l.; for use, 2 ml. of glacial acetic acid are added to 100 ml. of this solution, which is used hot, since benzoic acid separates at room temperature. (iv) Ammoniacal tartrate solution: 30 g. of tartaric acid and 150 ml. of ammonia (*d* 0·88) in 1 l. (v) Ammonium sulphide–tartrate wash-liquid: a solution of 1 g. of tartaric acid in 200 ml. of water is saturated with hydrogen sulphide, and 2·8 ml. of ammonia (*d* 0·88) are added. (vi) "Oxine" reagent: 10 g. of 8-hydroxyquinoline are treated with 25 ml. of glacial acetic acid diluted with an equal volume of water and made up to 500 ml. (vii) Standard 0·1N-potassium bromate–bromide solution: 2·784 g. of potassium bromate and 13 g. of potassium bromide in 1 l. (1 ml. = 0·2248 mg. of aluminium). (viii) 0·1N-Sodium thiosulphate solution: 25 g. of the pentahydrate and 2 g. of borax in 1 l. (ix) Indigo-carmine indicator: 0·5 g. in 100 ml. of water. (x) Stabilised starch solution: 2 g. of soluble starch made into a smooth paste with a little cold water and poured with constant stirring into 500 ml. of boiling water containing 0·6 g. of salicylic acid; boiling is continued for 2 mins., and the solution cooled to room temperature.

Procedure.—For amounts of 0·02—0·1% of aluminium, 5 g. of fine magnetted drillings are gently heated in a 400-ml. conical beaker with 25 ml. of 1 : 4 sulphuric acid and 25 ml. of 1 : 9 hydrochloric acid. When the evolution of hydrogen has ceased, 1 g. of pure zinc is introduced, and the liquid warmed for 5 mins. The solution is then filtered through a 9-cm. Whatman filter-paper No. 41 into a 400-ml. conical beaker, and beaker and filter are washed five times with 10 ml. of water. The filtrate is cooled, and after addition of 4 ml. of solution (i), 5N-ammonia is added in portions of 1 ml. with constant shaking, until a distinct turbidity remains. To the turbid solution 3 or 4 drops of glacial acetic acid are added, but no attempt is made to dissolve the slight precipitate which collects at the bottom of the vessel. Slowly and with constant stirring, 20 ml. of reagent (ii) are added. The liquid is heated and kept gently boiling for 5 mins. with occasional stirring. The precipitate is allowed to settle somewhat and is then filtered hot on an 11-cm. Whatman filter-paper No. 41. If the first portion is turbid, it should be refiltered. After the beaker and filter have been washed five times with hot wash-liquid (iii) and once with hot water, the precipitate is dissolved on the filter-paper with 50 ml. of hot ammoniacal tartrate solution (iv), and the filter-paper washed with a hot mixture of 5 ml. of solution (iv) and 45 ml. of water.

The filtrate and washings, collected in the beaker in which the benzoate precipitation took place, are heated just below boiling point, and a rapid current of hydrogen sulphide is passed through for 5 mins. Half a macerated Whatman accelerator and 3 ml. of ammonia (*d* 0·88) are added, and after the solution has been shaken and gassed for 2 mins. the precipitate is allowed to settle in a warm place. It is then filtered off on an 11-cm. Whatman filter-paper No. 41, and beaker and filter are washed five times with 10 ml. of wash-liquid (v). The filtrate and washings are collected in a 400-ml. conical beaker, heated to 90°, and an excess of oxine reagent (vi) (shown by a yellow colour of the liquid) is added slowly and with constant stirring. Heating at 90° is continued until the precipitate coagulates, and it is allowed to settle

in a warm place for 15 mins. The complex is then collected on an 11-cm. Whatman filter-paper No. 540, and beaker and filter are washed with hot water until the washings are colourless. The precipitate is dissolved on the filter with 50 ml. of hot 1 : 1 hydrochloric acid into the beaker in which the oxine precipitation took place, and the filter is washed with 50 ml. of hot water. The volume is adjusted to 150 ml., and the solution cooled to room temperature. After addition of three drops of indicator (ix), standard bromate–bromide solution is run in slowly from a burette until the colour changes to pure yellow, and then 3—5 ml. are added in excess. About 1 g. of potassium iodide is introduced, and the liberated iodine is titrated with thiosulphate solution, 5 ml. of starch solution being used as indicator. The thiosulphate solution is standardised against the bromate–bromide solution. Correction is made for the bromine consumption of the indicator; for this purpose, the same amount of the indicator solution as used in the estimation is added in a " blank " titration. The time for the estimation is 2½ hours.

Results.—All experiments were carried out upon 5·000 g. of Prime Western Spelter of the following composition: lead, 1·05; iron, 0·015; tin, 0·01; cadmium, 0·18%; remainder, zinc. Various amounts of pure aluminium were added, and the results are shown in the following table.

Aluminium taken:		Titration.				
g.	*i.e.*, % on 5-g. sample.	0·1N-$KBrO_3$–KBr, ml.	0·1N-$Na_2S_2O_3$, ml.	Diff., ml.	Al, found, g.	Error, g.
Nil	Nil	—	—	—	Nil	—
0·0012	0·024	9·05	4·60	4·45	0·0010	−0·0002
0·0024	0·048	15·95	4·85	11·10	0·0025	+0·0001
0·0036	0·072	19·85	4·30	15·55	0·0035	−0·0001
0·0048	0·096	25·00	4·10	20·90	0·0047	−0·0001

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MANOR WORKS, BRAINTREE, ESSEX. [*Received, January 19th*, 1945.]

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80. *The Metal-catalysed Reaction between Acetylene and Hydrogen. Part III. Some Effects of Added Substances on the Reaction over Nickel.*

By J. SHERIDAN.

Reaction over nickel on a number of carrier substances (chiefly oxides) differs little from that over nickel–pumice. No influence of carbon dioxide or nitrogen is detected. More than *ca.* 3% of nitric oxide retards reaction and lowers the yield of ethylene slightly; liquids containing nitrogen are formed. Some reduction of nitric oxide by hydrogen probably occurs. Oxygen retards reaction and raises the ethane yield. It is removed partly as water, but also reacts with the catalyst, its effects persisting during several succeeding experiments.

Silica, titania, thoria, zinc oxide, and chromium sesquioxide catalyse polymerisation in acetylene alone at 200° or below.

THE acetylene–hydrogen reaction on nickel has been studied with various catalyst carriers, chiefly kieselguhr (*e.g.*, Yoshikawa, *Bull. Chem. Soc. Japan*, **1932**, **7**, 201; Pichler, *Ges. Abh. Kennt. Kohle*, **1934**, **11**, 395; Ackermann, *Brennstoff-Chem.*, **1937**, **18**, 357); with this carrier, as with unsupported nickel, reaction appears to be little different from that on nickel–pumice (Parts I and II, J., 1944, 373; this vol., p. 133). With more reactive supports, such as zinc chloride or phosphoric acid, a considerable influence of carrier and metal : carrier ratio is reported (Petrov and Antsus, *Bull. Acad. Sci. U.R.S.S.*, Classe sci. chim., 1940, 274). An influence of metal dispersity with a kieselguhr base (Yoshikawa, *loc. cit.*) remains unconfirmed. Little is known of the effects of oxides as carriers, and further study of these is now reported. In supplement to this, the effects of various oxides on acetylene alone have been examined, since the few previous data usually do not provide clear evidence of the influence of such substances at temperatures below *ca.* 350° (see, *e.g.*, Egloff, " The Reactions of Pure Hydrocarbons," 1937, p. 442).

Dilution with, *e.g.*, carbon dioxide, nitrogen, methane, or steam has been claimed to raise the yields of C_2 hydrocarbons from acetylene and hydrogen over cheap catalysts such as nickel (U.S.P. 1,308,777; D.R.-PP. 350,429, 552,008; cf. D.R.-P. 262,541). The effects are unconfirmed unless they consist simply in prevention of overheating of the catalyst (*e.g.*, Dupont and Lombard, *Bull. Soc. chim.*, 1941, **8**, 851). Further tests leading to this conclusion, and also the effects of nitric oxide and oxygen, are now reported.

EXPERIMENTAL.

Gases.—For flow experiments, cylinder acetylene was passed through towers containing concentrated sodium bisulphite and aqueous sodium hydroxide. Hydrogen, and the acetylene for other experiments, were as described in Part I. Nitric oxide was prepared by the action of ferrous sulphate solution on a mixture of concentrated sulphuric acid and potassium nitrate. Other gases were obtained from cylinders.

Catalysts.—(For metal : carrier ratios, see note to Table I.) The nickel–pumice catalysts were those described in Part I. The catalyst on commercial activated alumina was made in an analogous manner, the final reduction being by hydrogen and methanol vapour at 350—400° for 3 hrs. Water-glass was added to certain catalysts to make them sufficiently coarse for use in flow experiments; nickel nitrate solution was evaporated in the presence of the appropriate oxide (commercial grade), water-glass solution evaporated in the presence of the product, and the residue heated to 300—350° for several hours. Catalyst 2 (see Table I) was reduced by ethanol vapour in nitrogen at 400° for 2—3 hrs., catalyst 3 by hydrogen containing ethanol vapour at 400° for 2 hrs. Others containing water-glass were reduced by hydrogen containing methanol vapour at 350—400° for 3 hrs. This treatment will reduce vanadium pentoxide to the tri- or tetr-oxide. Catalysts on precipitated alumina were made by two methods: (1) (adapted from Zelinsky and

Kommarevsky, *Ber.*, 1924, **57**, 667) aluminium nitrate was treated with sodium hydroxide till the precipitate was just redissolved, nickel nitrate solution added, and the mixture saturated with carbon dioxide; the precipitate was washed, dried, ignited, and reduced in hydrogen at 300° for 12 hrs.; (2) mixed solutions of nickel and aluminium nitrates were treated at 50—55° with sodium hydroxide, and the dried precipitate (a hard gel) heated to 400° in nitrogen and reduced as in (1).

For tests of their effect on acetylene alone, gels of alumina, silica, titania, chromium sesquioxide, and zinc oxide were prepared as follows (the titania and zinc oxide were kindly supplied by Dr. P. H. Given): (*a*) treatment of aluminium nitrate (50% soln.) at 50—55° with the equivalent of 6% sodium hydroxide; (*b*) treatment of commercial sodium silicate (in 20% soln.) at *ca.* 50° with *ca.* one-third of its weight of hydrogen chloride as 2·3% solution; (*c*) dropping titanium tetrachloride into 10% ammonia and boiling the product; (*d*) treatment of chromic nitrate (6%) at 78—84° with slight excess of 17% ammonia, followed by dilution and boiling; (*e*) treatment of a cloudy 5·7% solution of zinc chloride (600 c.c.) at 40—63° with 425 c.c. of 5·9% sodium hydroxide, followed by dilution and boiling. The precipitates were washed and dried in air or nitrogen, usually at 300—350°. Specimens (2—4 g.) of these oxides, and also of commercial thoria and acid-washed kieselguhr, were finally heated to 300° under high vacuum in the reaction bulb until their water-vapour pressures were very small.

Apparatus.—For constant volume runs this was the same as in Part I. The flow apparatus was mainly of all-glass type. Gases (from flow-meters) were mixed in a tower over alkaline pyrogallol, and traversed 3—5 g. of catalyst in the central 10 cm. of a 40-cm. electrically heated tube (1 cm. diam.). A coated thermocouple, in the catalyst, recorded the temperature. After passing through a trap at *ca.* −10° (and sometimes one at −78°), gases were collected at constant pressure (*ca.* 1 atm.) over saturated salt solution. Flow-meters were calibrated as described by Meuron (*Ind. Eng. Chem. Anal.*, 1941, **13**, 114). Errors due to solubility of acetylene were minimised by driving that gas, during calibration, with saturated salt solution, kept fully saturated with acetylene by suitable precautions, and also by transferring gases awaiting analysis, under slight excess pressure, to bulbs isolated from the salt solution. All flow-rates were converted to terms of dry gas at N.T.P. Exothermic reaction was usually evident over catalysts pre-heated to 350° in hydrogen. After the steadiest possible conditions had been maintained for *ca.* 1 hr., approximately 1 l. of gas was collected. The rate of collection often increased during a run, on account of a decline in catalyst activity. For a large extent of reaction in these runs, a maximum error of *ca.* ±3% (of the unrecovered acetylene) in the ethylene yield appears reasonable, with ±1% for the smaller ethane yields.

Gas Analysis.—Carbon dioxide was absorbed before the usual analysis (see Part I). Tests for nitric oxide were made by adding a measured excess of oxygen and exposing the gases to potassium hydroxide.

Results and Discussion.

(i) *Influence of Catalyst Carrier.*—The results are summarised in Table I, the contact times being *ca.* 2—6 secs. (in all tables, C_mH_n represents unsaturated hydrocarbons higher than the C_2 series). On kieselguhr–water-glass (catalysts 2 and 3) the yields of C_2 hydrocarbons (as fractions of the unrecovered acetylene) seem slightly higher than on pumice (catalyst 1); ethylene is the chief C_2 product, as with all the carriers tested. On activated alumina (catalyst 4) the lowest ethylene yield is recorded. On precipitated alumina (catalysts 5 and 6) the yields resemble those on catalysts 1—3, as was confirmed for catalyst 6 by experiments at constant volume at 17—105°. On vanadium oxide–water-glass (catalyst 7) the yields resemble those with pumice, but a lower ethylene yield is recorded on chromium sesquioxide–water-glass (catalyst 8).

The group of three runs over catalyst 5 in Table I are successive 1-hr. stages of one experiment; the yields are little affected by decreasing activity of the catalyst.

Catalyst 4 had little effect on acetylene alone in *ca.* 6 secs. at 170° (Table I); catalyst 5 caused rapid decomposition of acetylene at 316°.

Over all catalysts, products other than C_2 hydrocarbons account for removal of more acetylene than

Table I.

Flow experiments over nickel on different carriers.

Catalyst No.*	Temp. (±5°).	Flow rates (l./hr.). C_2H_2.	H_2.	Gaseous product.	Product (vol. % to nearest unit %). C_2H_2.	C_mH_n.	C_2H_4.	H_2.	C_2H_6.	% C_2H_2 reacted.	Yield (%). C_2H_4.	C_2H_6.
1	178°	1·06	1·00	0·67	10	12	52	16	7	94	35	5
2	177	2·70	2·41	1·89	20	12	53	6	7	86	43	5
	183	2·73	2·47	1·94	20	14	50	5	7	86	41	6
	130	2·84	2·53	2·00	17	13	53	7	8	88	42	6
	131	2·85	2·56	2·01	18	13	53	6	9	87	43	7
2	212	2·39	2·50	1·80	7	13	54	14	11	95	43	9
	214	2·42	2·57	1·82	6	13	54	14	10	95	43	8
3	141	1·12	1·03	0·96	25	8	41	18	7	79	45	7
4	147	1·36	1·25	0·54	9	1	48	15	23	96	20	9
	170	2·23	—	2·13	97	—	1	—	—	—	—	—
5	150	1·32	1·27	0·63	1	1	76	4	16	99	36	8
5	150	1·43	1·34	0·74	5	1	72	7	14	97	38	7
	150	1·43	1·32	0·77	12	1	67	8	11	94	39	6
	150	1·43	1·28	0·93	21	1	56	11	9	86	42	7
6	150	1·17	1·17	0·78	23	1	39	24	10	84	31	8
7	140	1·46	1·47	0·83	3	1	60	25	10	98	35	6
8	138	1·54	1·43	0·70	3	1	54	31	9	99	25	4

* Numbering of catalysts (weight-ratios are given).—1 = 1 nickel : 10 pumice; 2 = 3 nickel : 10 kieselguhr : 10 water-glass; 3 = 2 nickel : 10 kieselguhr : 10 water-glass; 4 = 1 nickel : 5 commercial activated alumina; 5 = 2 nickel : 5·5 precipitated alumina (method 1); 6 = 1 nickel : 8·5 precipitated alumina (method 2); 7 = 2 nickel : 10 water-glass : *ca.* 10 vanadium oxide; 8 = 2 nickel : 10 chromium sesquioxide : 10 water-glass. Brackets against catalyst numbers embrace experiments made on the same specimen of catalyst.

hydrogen (acetylene : hydrogen ratio in these products = 1·1—1·5). Removal of acetylene in this form can be favoured, *e.g.*, by alumina or chromium sesquioxide; this is probably related to the effects of such oxides themselves on acetylene (see below). The structures of the products other than C_2 hydrocarbons may be influenced by the catalyst carrier, but in the cases listed there is a general resemblance to reaction over nickel–pumice.

Tests were also made of the action of some possible catalyst supports on acetylene alone at 17—384°. Table II summarises a comparison of reaction in acetylene in a Pyrex bulb with that in the presence of various oxides (Δp = pressure-fall measured at constant volume; t = duration in mins.). The last col. records the phenomena observed on withdrawing the gas.

TABLE II.

Catalyst.	Temp.	Initial press. of C_2H_2 (mm.).	Δp.	t.	% C_2H_2 in product gas.	
None	445°	520	75	35	97	Fog
Kieselguhr	384	495	27	36	98	Slight fog
Al_2O_3	276	425	100	19	96·3	No fog
	313	490	440	15	—	—
SiO_2	356	495	208	21	94	Fog
	308	450	115	25	97	No fog
TiO_2	115	406	130	30	99	No fog
	267	474	210	7	97	Slight fog
ThO_2	98°	392	78	11	98·7	No fog
	180	455	118	11	98·9	No fog
Cr_2O_3	185	417	145	30	97·4	No fog
	230	432	163	6	95·4	No fog
ZnO	257	492	102	16	98	Fog
	316	502	215	28	94	Fog

Without a catalyst, reaction was very slow below 350—400°, and at 445° was mainly polymerisation; hydrogen, if added, acted chiefly as a diluent. Kieselguhr produced at the most a slight acceleration, but all the other substances induced reaction (predominantly polymerisation, with production of only traces of other gases) under conditions which leave acetylene unchanged for long periods. The active substances all adsorbed *ca.* 2—6 c.c. of acetylene (at N.T.P.) per g. at *ca.* 400 mm. and 20°. As the temperature was raised, adsorption decreased, and was eventually followed by a slower continued fall in pressure due to polymerisation, which was readily detected at *ca.* 100° for titania, thoria, and chromium sesquioxide and *ca.* 200° for alumina, silica, and zinc oxide. The oxides became discoloured by adsorbed hydrocarbons and, in time, less active in polymerising acetylene. No free carbon was found, except possibly with titania, which became black throughout the granules, though polymerisation was still the main reaction.

The results with alumina confirm those of Boswell and Dilworth (*J. Physical Chem.*, 1925, **29**, 1489). Stannous oxide has a similar effect (Pearce and Goergen, *ibid.*, 1928, **32**, 1423). Berl and Hofmann (*Z. angew. Chem.*, 1931, **44**, 259) reported that silica (and also stannic and calcium oxides) favoured decomposition rather than polymerisation; decomposition and polymerisation were reported over zinc oxide on charcoal at 370°. The somewhat different results of the present research (cf. also B.P. 334,203) may be in part due to differences in conditions. The effects of titania, thoria, and chromium sesquioxide have not been previously investigated.

The suggestion (Morris and Reyerson, *J. Physical Chem.*, 1927, **31**, 1332) that ethylene production from acetylene and hydrogen is favoured by a carrier substance (*e.g.*, silica) which adsorbs acetylene more strongly than hydrogen is probably unjustified, since it is based on the view that strongly adsorbed hydrogen and weakly adsorbed acetylene react on the metal, whereas the reverse is true on all metals on which the reaction kinetics are known. Even at the surface of palladium, acetylene is the more strongly adsorbed reactant (Fischer and Knorr, *Z. Elektrochem.*, 1937, **43**, 608; Cremer, Knorr, and Plieninger, *ibid.*, 1941, **47**, 737), and it seems unlikely that any added substance will greatly favour hydrogen adsorption relative to acetylene adsorption, though this might decrease the yield of reduced polymers of acetylene. Conversely, substances which induce polymerisation of acetylene, or even adsorb that gas strongly, are probably to be avoided as catalyst carriers if high yields of C_2 hydrocarbons are desired, though their effect may not be large in the time of reaction (cf. Table I).

(ii) *Effects of Carbon Dioxide and Nitrogen.*—It was shown by experiments at constant volume that large proportions of carbon dioxide had scarcely any influence on the rate or products of the acetylene–hydrogen reaction at 79° over nickel–pumice. Nitrogen also behaved as an inert diluent in flow experiments.

(iii) *Effect of Nitric Oxide.*—Table III summarises results over nickel–kieselguhr–water-glass catalysts under conditions similar to those of the runs in Table I, but with nitric oxide added (the nitric oxide contents are given as volume percentages of the mixed gas before reaction).

More than *ca.* 1—2% of nitric oxide in the mixture caused some suppression of reaction. The yields of ethylene were depressed slightly by 3·6—6·5% of nitric oxide, but those of ethane were little affected (cf. Table I). The gaseous products contained no appreciable nitric oxide. The liquid products contained nitrogen, were darker than those obtained in the absence of nitric oxide, and had a most unpleasant odour. Ammonia and water were also formed.

These facts suggest that the nitric oxide is reduced by hydrogen, ultimately to ammonia (Neogi and Adhicary, *Z. anorg. Chem.*, 1910, **69**, 209; Guye and Schneider, *Helv. Chim. Acta*, 1918, **1**, 33). No reaction between acetylene and nitric oxide was detected in short contact times over the same catalysts at *ca.* 200°. In the presence of hydrogen, some nitric oxide may have been removed in terminating radical polymerisation chains on the catalyst (cf. Part II; such termination can apparently occur in gaseous acetylene polymerisation—see,

e.g., Burnham and Pease, *J. Amer. Chem. Soc.*, 1942, **64**, 1404), but the failure of nitric oxide to raise the yield of C_2 hydrocarbons does not support this. The capacity of nitric oxide for destroying free radicals may well be removed if that gas is chemisorbed. Nitrogen may enter the organic products at some stage during the

TABLE III.

Effect of nitric oxide on flow experiments over nickel–kieselguhr–water-glass catalysts.

Catalyst No.*	Temp. (±5°).	Flow rates (l./hr.). C_2H_2.	Flow rates (l./hr.). H_2.	NO, %.	Gaseous product rate (l./hr.).	Product (vol. % to nearest unit %). C_2H_2.	C_mH_n.	C_2H_4.	H_2.	C_2H_6.	% C_2H_2 reacted.	Yield (%). C_2H_4.	Yield (%). C_2H_6.
2	229°	2·40	2·63	1·2	1·88	6	12	47	23	9	95	39	7
	229	2·36	2·63	1·2	2·04	11	11	40	27	8	90	38	8
	169	2·64	2·74	6·5	2·56	30	7	23	32	6	71	32	8
	169	2·71	2·77	6·3	2·72	32	7	21	32	5	68	32	7
	180	1·26	1·06	3·6	0·85	24	11	42	9	8	84	34	6
3	182	1·07	0·96	2·5	1·33	40	5	17	34	3	50	42	6

* See footnote to Table I.

reduction of nitric oxide. Thus acetylene and ammonia condense under a variety of conditions, though these are usually more vigorous than in the present work (see, *e.g.*, Berkman, Morrell, and Egloff, " Catalysis," 1940, p. 945).

Although the mechanism of the effect of nitric oxide is therefore uncertain, quite small amounts can clearly be adsorbed and react. Their influence is reminiscent of that of carbon monoxide, 2% or more of which is reported to retard acetylene removal and to raise the yield of liquid products considerably (Binnie, *J. Soc. Chem. Ind.*, 1931, **50**, 297).

(iv) *Effect of Oxygen.*—Less than *ca.* 10 mm. of air had little effect on reaction over nickel–pumice, but more than this amount (or its equivalent of oxygen alone) depressed the rate of fall in pressure at constant volume ($-dp/dt$), without, however, changing the general shape of the pressure–time curves; *i.e.*, no induction period or marked rise in $-dp/dt$ at any stage was found. The retardation increased with the amount of oxygen.

Table IV gives numerical data on this effect. In run 62, $-dp/dt$ was reduced to *ca.* one-fifth of its value in runs 59—61 by 54 mm. of air, and the retardation was almost as great in run 63, with no air admitted. In runs 64—66 (not shown), under the same conditions as run 63, $-dp/dt$ returned in stages to about that of runs 59—61. In the second group, 11·5 mm. of oxygen (run 36) depressed $-dp/dt$ to *ca.* one-quarter of its value in run 35, and 22 mm. (run 38) depressed it to *ca.* one-twelfth of that value. Recovery of the original rate was again spread over several runs.

The pressures in the gaseous product and yields in Table IV are maximum values, no products being supposed to condense before the gas is analysed. Inspection shows that when oxygen is added the resultants other than C_2 hydrocarbons must contain an unusually high proportion of hydrogen, which suggests water

TABLE IV.

Effects of air and oxygen on reaction.

Temp. = 83°. Each group of experiments over different samples of nickel–pumice (metal : pumice ratio 1' : 10).

Expt. no.	Initial press. (mm.). H_2.	C_2H_2.	O_2.	Δp.	t.	Max. press. (mm.) in gaseous product. C_2H_2.	C_mH_n.	C_2H_4.	H_2.	C_2H_6.	O_2.	CO_2.	CO.	Maximum yield (%). C_2H_4.	Maximum yield (%). C_2H_6.
59	400	206	—	206	22	63	10	60	237	13	—	—	—	42	9
60	395	203	—	202	23	63	12	56	237	14	—	—	—	40	10
61	397	198	—	200	21	61	11	55	242	13	—	—	—	40	9
62	400	203	54*	160	111	105	5	38·5	249	35	2	3	2	39	35
63	400	200	—	299	193	4	12	73	139	59	—	0	—	37	30
35	298	302	—	301	28	94	13	78	94	13	—	—	—	38	6
36	302	299	11·5	300	108	110	14	76	74	28	0	2	2	40	15
37	302	300	—	300	35	93	13	82	83	21	—	—	—	40	10
38	300	301	22	304	324	132	12	68	49	47	1	3	3	40	28
39	297	300	—	301	62	96	15	80	65	35	—	2	2	38	17
40	299	302	—	301	39	97	16	81	76	25	—	—	—	39	12
41	300	302	—	300	31·5	93	17	78	83	19	—	2	1	38	9

* Air, not oxygen.

formation, since oxides of carbon will account for, at most, a small proportion of the oxygen removed. The yields of ethylene and ethane (but not their ratio) would then be lower than those tabulated. Their minimum values (estimated by assuming a water vapour pressure equal to twice the initial oxygen pressure) are, for run 62, 36% of ethylene and 33% of ethane, for run 36, 36% and 13%, and for run 38, 32% and 21%, respectively. The true yields will lie between these values and those in Table IV, since some oxygen is probably removed as oxides of carbon, and some almost certainly by combination with the catalyst, otherwise its effects would not extend to subsequent runs without oxygen, during which this inhibitor must be slowly removed from the nickel. If water is formed in such removal, small corrections to other yields will be necessary.

When these considerations are taken into account, there is no doubt that the yield of C_2 hydrocarbons, which in run 35 had its exepcted value for a catalyst not previously exposed to oxygen, is raised by oxygen. The increase is essentially in the ethane yield, and runs parallel with the retardation; as $-dp/dt$ increases again (*e.g.*, in runs 39—41) the ethane yield moves towards its value in unretarded runs. The yields of C_2 products in runs 59—61 are slightly larger than expected, probably because several runs with added air were included in nos. 47—58 of the same series.

It is clear that small amounts of oxygen are sufficiently strongly adsorbed to influence the reaction considerably, despite the strong adsorption of acetylene; the total inhibition of hydrogenation by oxygen, found with ethylene on nickel (Rideal, J., 1922, **121**, 309), is not observed. Mechanisms can be suggested for the phenomena with acetylene, though definite conclusions cannot be reached. Thus the change of yield might be related to a lowering of surface concentration of acetylene by oxygen adsorption, the chance of two acetylene molecules combining being lowered; a lowering of acetylene adsorption in proportion to the fall in rate (*e.g.*, to $\frac{1}{6}$—$\frac{1}{12}$ of its normal value), however, would probably make this chance very small, though much acetylene is still removed as products less volatile than C_2 hydrocarbons. Displacement of hydrogen may well also play a part, therefore, in the retardation. Another possibility is that oxygen is more strongly adsorbed at sites normally tending to favour polymerisation, than at others which normally favour the simple hydrogenation. The elevation of ethane production suggests that acetylene and ethylene are more nearly equally strongly adsorbed on the poisoned surface, possibly on account of a preference of oxygen for sites normally adsorbing acetylene, or some lattice modification induced by oxygen.

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81. *The Metal-catalysed Reaction between Acetylene and Hydrogen. Part IV. Reaction over Platinum.*

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Ethylene is not formed selectively from acetylene and hydrogen over platinum–pumice at 0—163°, though acetylene is more strongly adsorbed than ethylene, and at pressures above a low value (which depends on the pressures of hydrogen and ethylene present) inhibits ethane production to a rate less than, but comparable with, that of ethylene formation. With 1 : 1 and 2 : 1 hydrogen : acetylene mixtures some 6—30% of the acetylene not recovered, and a comparable amount of hydrogen, are removed as products less volatile than C_2 hydrocarbons, though the catalysts are virtually without action on the same partial pressures of acetylene alone at those temperatures. Previous kinetic data are confirmed and amplified, and it is shown that lower temperatures favour ethane production in the early stages. The reactions (I) $C_2H_2 + H_2 = C_2H_4 (\rightarrow C_2H_6)$ and (II) $C_2H_2 + H_2 \longrightarrow$ products other than C_2 hydrocarbons are probably both of approximately first order with respect to hydrogen, and have similar heats of activation [that of (II) being the higher by *ca.* 1—2 kg.-cals.] in the region of 12 kg.-cals. The differences between (I) and (II) are qualitatively the same as for the corresponding reactions over nickel. The stronger adsorption of acetylene than of ethylene is confirmed by the fact that ethylene added to the system acts primarily as a diluent. Oxygen has little effect on the reaction, though some water is formed.

ACETYLENE and hydrogen react over platinum to give ethylene and ethane (von Wilde, *Ber.*, 1874, **7**, 353; Sabatier and Senderens, *Compt. rend.*, 1900, **131**, 40; Paal and Schwarz, *Ber.*, 1915, **48**, 1202; Morris and Reyerson, *J. Physical Chem.*, 1927, **31**, 1332; Lebedev, Gulyaeva, and Vasil'ev, *J. Gen. Chem. U.S.S.R.*, 1935, **5**, 1422). At lower temperatures acetylene is removed almost entirely as these two gases, and reaction is quantitative with a large excess of hydrogen (Conn, Kistiakowsky, and Smith, *J. Amer. Chem. Soc.*, 1939, **61**, 1868); at higher temperatures (*e.g.*, 180°), and with greater proportions of acetylene, some less volatile hydrocarbons are formed.

The statement (Farkas, *Trans. Faraday Soc.*, 1939, **35**, 908) that acetylene and hydrogen do not react over platinum unless the hydrogen pressure is the greater is not confirmed by the results of Farkas and Farkas (*J. Amer. Chem. Soc.*, 1939, **61**, 3396), though the kinetics found by these authors indicate reaction between strongly adsorbed acetylene and weakly adsorbed hydrogen. An increase in the rate of fall in pressure (at constant volume) was observed in hydrogen-rich mixtures after a fall in pressure roughly equal to the initial acetylene pressure. Reaction up to this point was regarded as exclusively $C_2H_2 + H_2 = C_2H_4$, ethane formation being completely suppressed, on account of the stronger adsorption of acetylene than ethylene, until all or almost all, the acetylene had been removed, after which a faster hydrogenation of ethylene developed. Acceleration of hydrogenation, regarded as coincident with total acetylene removal, was observed by Lebedev, Gulyaeva, and Vasil'ev (*loc. cit.*); they considered that some ethane was formed at earlier stages, a view supported by results of other workers mentioned. In view of this, and since the course of reaction advocated by Farkas and Farkas was apparently proposed without support from analyses of hydrocarbon products, further kinetic study in conjunction with full gas-analyses has been made.

Experimental.—Experiments were performed at constant volume, the gases (except oxygen, which was taken from a cylinder) and apparatus being those described in Part I (J., 1944, 373). The catalysts were carried on the same pumice base as there described, and had platinum : pumice ratios of 1 : 250 (Pt-1) and 1 : 10 (Pt-2). Pt-1 was made by dissolving platinum in aqua regia, diluting the solution, and evaporating it in the presence of pumice. When, as here, the

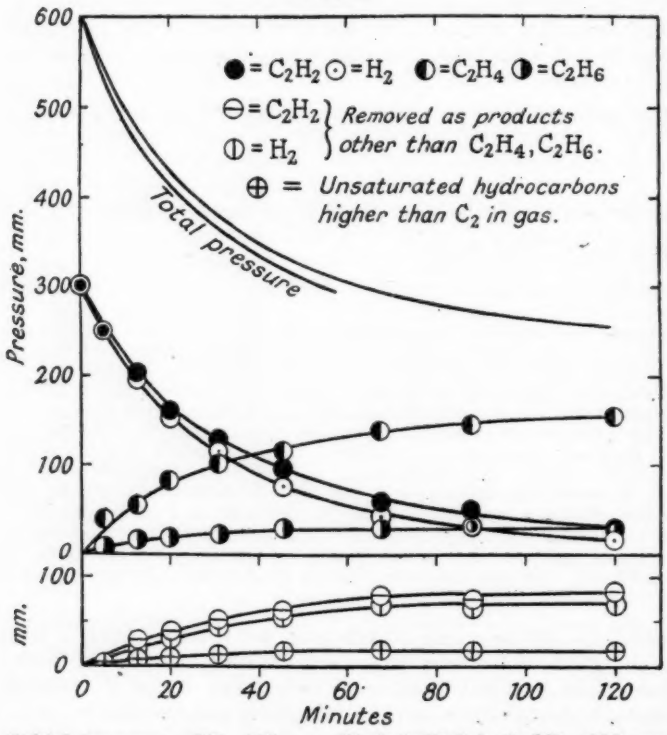
nitric acid was not removed by repeated partial evaporation, catalysts so made were not highly active, even with a 1 : 10 metal : pumice ratio. After brief ignition in a dish, the platinic chloride was decomposed as required in the reaction bulb by heating it to 300—350° for *ca.* 1 hr. at 10 mm. pressure and then in 400—500 mm. of hydrogen at the same temperature for several hours. The catalyst was cooled in hydrogen or in a vacuum, and not allowed to come into contact with air during use. Pt-2 was made by evaporation of a solution of platinic chloride in the presence of pumice, followed by the same treatment as for Pt-1. The mass of catalyst used for each series of experiments was 2 g. for Pt-2 and 1 g. for Pt-1. Runs were numbered in order of performance over each specimen of catalyst, the order being such that any variations in catalyst activity could not lead to false conclusions about the effects of conditions on the reaction.

Gases were analysed as outlined in Part I (*loc. cit.*) and Part III (preceding paper). The saturated hydrocarbon contents were found by oxidation over copper oxide at 600° to have a mean composition almost exactly C_2H_6, and the ethane contents were taken as the same as the saturated contents.

Results and Discussion.

(i) *Activity of Catalysts and their Effect on Acetylene Alone.*—Pt-1 retained a fairly constant activity for the acetylene–hydrogen reaction during long series of experiments at 140—165°, but Pt-2, initially much more active, retained a high and steady activity only during the removal of *ca.* 0·1 g. of acetylene per g. of catalyst within the first few hours of its use, after which it became progressively less active. No marked increases in activity were observed and no dependence of the products on the activity of the catalysts was apparent.

Fig. 1.



Initial pressures: 298—301 *mm.* H_2 (*admitted first*), 298—306 *mm.* C_2H_2. *See Table I(a). The limits of variation of total pressure curves are shown.*

Both catalysts were without measurable action on acetylene alone at the temperatures and partial pressures at which acetylene and hydrogen formed some products less volatile than ethylene and ethane. A pressure fall was not observed in the absence of hydrogen until considerably higher temperatures were reached, *e.g.*, with 302 mm. of acetylene over Pt-1 at 353° the pressure fell 15 mm. in 20 mins., the gas, after separation of slight fog, then containing 97·8% of acetylene.

(ii) *The Course of Reaction at Constant Volume.*—This was determined by the method used for nickel catalysts (Part I), runs of different durations being made under the same conditions, and the analytical results plotted at time co-ordinates equal to the times required for the appropriate pressure falls in the longest experiment of each series; this is equivalent to a correction to constant catalyst activity (cf., *e.g.*, Twigg and Rideal, *Proc. Roy. Soc.*, 1939, *A*, **171**, 55; Twigg, *ibid.*, 1941, *A*, **178**, 106). Figs. 1 and 2 show the results for 1 : 1 and 2 : 1 hydrogen : acetylene mixtures over Pt-1 at 163° and 145°, respectively. The yields, in terms of the acetylene not recovered, are given in Table I, (*a*) and (*b*). Despite some variation in catalyst activity, smooth curves are obtained for the partial pressures, etc., and there is no reason to doubt that the course of reaction in the longest experiment is close to that plotted.

With both gas ratios, hydrogen is more rapidly removed than acetylene, and some ethane is formed almost from the start. Ethylene production is 4—5 times as fast as ethane formation in the 1 : 1 gas mixture, and about twice as fast in the early stages of reaction in the 2 : 1 hydrogen : acetylene mixture. In Fig. 1, as in all reactions with 1 : 1 mixtures, the rate of fall in total pressure ($-dp/dt$) decreases continuously throughout. In Fig. 2 the increase in $-dp/dt$ is first detected when the total pressure fall (Δp) is roughly equal to the initial acetylene pressure, as is seen from Fig. 4 (curve 1). The acceleration coincides roughly with the beginning of an increase in rate of ethane formation and a slowing of ethylene production, the gas at the commencement of the acceleration containing approximately: H_2, 210; C_2H_2, 60; C_2H_4, 72; C_2H_6, 42 mm. The value of $-dp/dt$ then passes through a maximum, roughly coincident with the maximum in ethylene pressure; at this point there are present some 137, 10, 82, and 74 mm., respectively, of the above gases. The remainder of the reaction is mainly $C_2H_4 + H_2 = C_2H_6$, the acetylene pressure falling almost to zero.

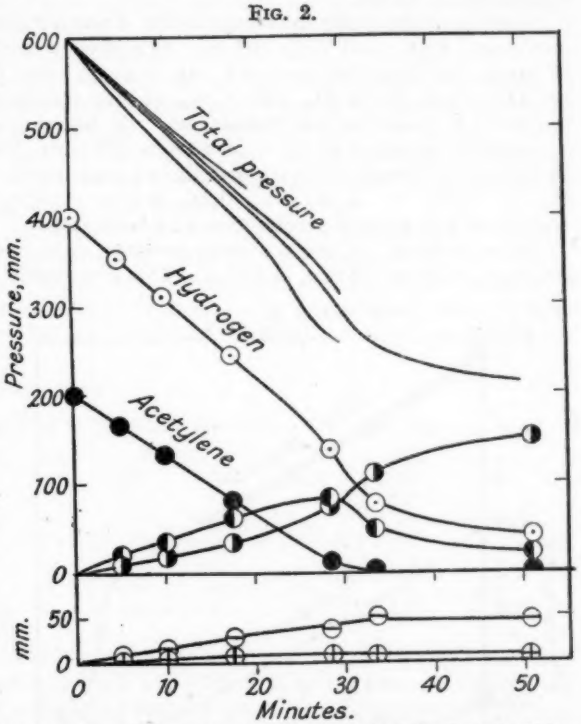
The yields of C_2 hydrocarbons were 68—73% for 1 : 1 and 78—85% for 2 : 1 hydrogen : acetylene ratios at all stages of reaction. These values are a little too high because, first, slight fog formation occurred on

withdrawing gas, and secondly, acetylene being admitted after hydrogen, a fast initial reaction may have occurred while the acetylene pressure at the catalyst surface was very small (see below), making the recorded initial acetylene pressure too low. In view of the higher products already included in the gas pressures, and of the fact that *ca.* 100 mm. of acetylene were admitted in 1 sec., the true yields cannot be much less than those listed. Not more than a small part of the ethane production in the early stages can be due to the fast initial reaction mentioned, since ethane production continues when diffusion equilibrium is established and also occurs when acetylene is introduced first (see below).

Roughly equal amounts of acetylene and hydrogen are removed as products less volatile than ethylene and ethane; the pressures of unsaturated hydrocarbons higher than the C_2 series are *ca.* $\frac{1}{7}$—$\frac{1}{4}$ of the pressures of acetylene so removed. The less volatile products are therefore largely of relatively low molecular weight, *e.g.*, C_4, C_6, and C_8 compounds. Their formation ceases as soon as all the acetylene is removed, while ethylene hydrogenation continues.

Fig. 3 and Table I (*c*) show the course and yields of reaction in a 2 : 1 hydrogen : acetylene mixture over Pt-2 at 57°. The pressures of unsaturated hydrocarbons higher than ethylene are negligible. The acceleration effect is more marked than in Fig. 2 and the yields of C_2 products are higher, the most accurate figures being 90—94%. The rate of ethane production is about half of that of ethylene formation at almost the earliest stage, and the two rates are almost equal after *ca.* 30 mins. After some 73 mins. ($\Delta p = 235$ mm.) an increase in $-dp/dt$ is first perceptible (Fig. 4, curve 2), the gas then containing: *ca.* H_2, 170; C_2H_2, 40; C_2H_4, 85; C_2H_6, 59 mm. The value of $-dp/dt$ then passes through a very sharp and high peak. At the time of the very large acceleration the acetylene pressure has fallen to some 10—20 mm.; it is clear that the ethylene pressure must pass through a sharp maximum at about this time, and that the very fast reaction is predominantly hydrogenation of ethylene. In harmony with the high ethane production, hydrogen is removed much more rapidly than acetylene from the earliest stages. Deactivation of the catalyst prevented more points being fixed, but the course of reaction must be close to that shown. The amounts of acetylene and hydrogen removed as products other than ethylene and ethane are roughly equal, but the possible errors are a large proportion of the small pressures concerned.

FIG. 2.



Initial pressures: 397—402 *mm.* H_2 (*admitted first*), 200—211 *mm.* C_2H_2. *See Table I*(*b*). *Significance of various types of point as in Fig.* 1 (*the amounts of* H_2 *removed as products other than* C_2H_4 *and* C_2H_6 *are not shown: they are equal within experimental error to the amounts of acetylene removed as such products*). *The limits of variation of total pressure curves are shown.*

Under the same conditions, over the same catalyst in a less active state, gas was analysed at $\Delta p = 330$ mm.

TABLE I.

Yields at different stages of reaction.

(*a*) In 1 : 1 H_2 : C_2H_2 mixture over Pt-1 at 163° (see Fig. 1).

No. of expt.	66	62	64	68	69	63	67	65
Duration (mins.)	5	11	20	30	45	60	90	120
Yield of C_2H_4, %	69	55	59	58	56	57	58	58
Yield of C_2H_6, %	14	16	13	13	14	11	12	12

(*b*) In 2 : 1 H_2 : C_2H_2 mixture over Pt-1 [same specimen as in (*a*)] at 145° (see Fig. 2).

No. of expt.	74	72	73	75	70	71
Duration (mins.)	5	10	20	30	30	51
Yield of C_2H_4, %	59	52	50	43	23	11
Yield of C_2H_6, %	26	27	28	38	55	71

(*c*) In 2 : 1 H_2 : C_2H_2 mixture over Pt-2 at 57° (see Fig. 3).

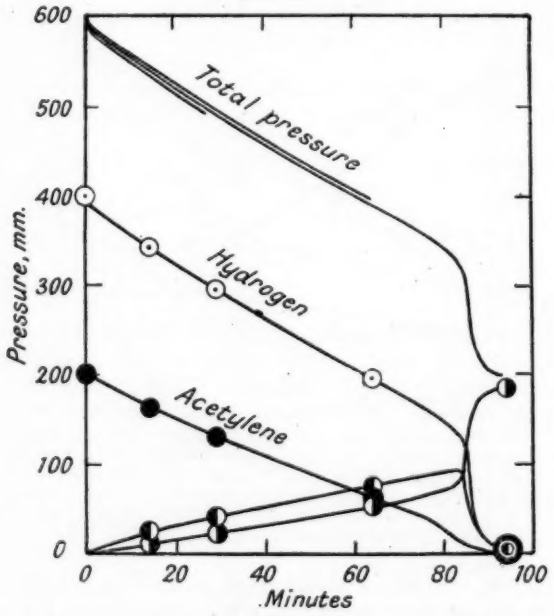
No. of expt.	5	3	4	2
Duration (mins.)	14	27	65	94
Yield of C_2H_4, %	53	60	54	2
Yield of C_2H_6, %	27	30	38	92

(189 mins.), $-dp/dt$ being about 2·5 times its initial value : H_2, 81; C_2H_2, 6; C_2H_4, 73; C_2H_6, 104 mm. (yields : C_2H_4, 38; C_2H_6, 54%). If deactivation of the catalyst is assumed to leave the relative speeds of the various reactions unchanged, these pressures can be taken as those for Δp = 330 mm. in Fig. 3 (*i.e.*, the region of the maximum in $-dp/dt$).

Further evidence for the course in Fig. 3 was obtained with a new sample of Pt-2 at 65° as follows (acetylene introduced first) : (*a*) With 199 mm. of acetylene and 399 mm. of hydrogen initially, gas was analysed after 67 mins., Δp being 263 mm. and $-dp/dt$ about twice its initial value and rising rapidly; the gas contained : H_2, 145; C_2H_2, 21; C_2H_4, 100; C_2H_6, 64 mm. (yields : C_2H_4, 56; C_2H_6, 36%); $-dp/dt$ in the residual gas was larger than before gas was withdrawn. (*b*) Starting with 42 mm. of acetylene and 100 mm. of hydrogen, an acceleration occurred at Δp = *ca.* 42 mm. (23 mins., Fig. 4, curve 3); whereas (*c*) with 42 mm. of acetylene and 98 mm. of hydrogen, the rate was almost unchanged, and after 10 mins. (Δp = 20 mm.) there were present : H_2, 78; C_2H_2, 27; C_2H_4, 9·4; C_2H_6, 3 mm. (yields : C_2H_4, 63; C_2H_6, 20%); reaction in the residual gas continued and showed acceleration at a later stage.

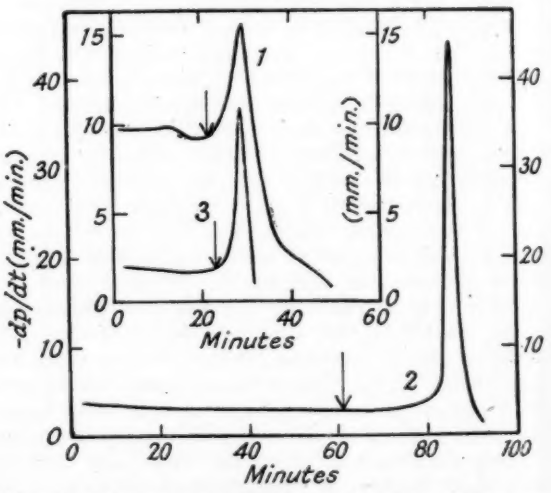
In experiment (*b*) the acetylene pressure must have fallen to 5—10 mm. before $-dp/dt$ began to rise, as compared with *ca.* 40 mm. in Fig. 3. This is probably due largely to the lower hydrogen pressure in the former

FIG. 3.



Initial pressures : 199—200 *mm.* C_2H_2 (*admitted first*), 399—410 *mm.* H_2. *See Table I(c). Significance of various types of point as in Fig.* 1. *The limits of variation of total pressure curves are shown.*

FIG. 4.



Curve 1 = *longest run in Fig.* 2; *curve* 2 = *longest run in Fig.* 3; *vertical arrows indicate the times when* Δp = *initial acetylene pressure.*

case [see (iii) below], though the ethylene pressure presumably also influences the time at which acceleration is first detected. Comparison of curves 2 and 3 in Fig. 4 suggests that, at lower total pressures, acceleration is observed at more nearly the point where Δp equals the initial acetylene pressure, but such an effect is probably also caused by an increase in hydrogen : acetylene ratio; with ratios from 3 to 6 (hydrogen pressure = 200—300 mm.) fast rates were observed, increasing before Δp reached the initial acetylene pressure.

The above courses of reaction can be explained only by a stronger adsorption of acetylene than of ethylene, this leading to a retardation of ethane formation until the acetylene pressure has fallen below a low value (which depends on the other pressures prevailing). Conclusions of this type reached by Farkas and Farkas (*loc. cit.*) are thus confirmed. All the experiments in the present paper, however, followed a course differing in some important respects from that postulated by those authors. First, ethane is produced virtually from the beginning in quantities less than, but of magnitude comparable with, those of ethylene, especially in mixtures rich in hydrogen. Thus the hydrogenation of ethylene, though retarded by, *e.g.*, some 50 mm. (or less) of acetylene to a rate only of the order of 1/100 of that expected in the absence of acetylene, is not inhibited so completely that the hydrogenation to ethylene can be described as selective. Secondly, the acceleration can begin and become marked at quite definite acetylene pressures.

The main argument used by Farkas and Farkas for selective ethylene formation appears to be that acceleration occurs suddenly when Δp equals the initial acetylene pressure. The suddenness of the phenomenon is perhaps open to question, but in any case the published total-pressure data of Farkas and Farkas differ little from some of the present results; *e.g.*, the accelerations were scarcely ever any more sudden than in curves 1

and 3 in Fig. 4, where $-dp/dt$ rises when Δp reaches the initial acetylene pressure; yet analyses show the course already described for these reactions. Acceleration at this particular point accordingly seems to be a coincidence due to compensation of two factors, *viz.*, definite ethane production and the presence of a definite acetylene pressure when acceleration begins. In many cases (*e.g.*, Fig. 4, curve 2) acceleration occurs after Δp exceeds the initial acetylene pressure; *i.e.*, the two factors do not balance. It is noted that the lower pressures and higher hydrogen : acetylene ratios of many of the experiments of Farkas and Farkas are conditions which seem to favour the occurrence of acceleration after a pressure fall nearer to the initial acetylene pressure, without giving rise to selective hydrogenation. The work of Farkas and Farkas was performed in the absence of pumice and probably with slightly purer gases than the present experiments, but it would be difficult to account for the early ethane production in the present work in terms of an inactive catalyst base or strong adsorption of even a reactive possible impurity, such as a trace of oxygen. The author therefore considers that at present there is no evidence of a truly selective hydrogenation of acetylene on platinum.

(iii) *Orders of Reaction.*—The effects of partial pressures on the initial rate of fall in total pressure, $(-dp/dt)_0$, over a specimen of Pt-2 (of fairly steady activity) at 73° are shown in Table II (hydrogen was admitted first). The apparent order with respect to hydrogen is *ca.* 1·2. With over 100 mm. of acetylene (in the presence of 300 mm. of hydrogen) the apparent order with respect to acetylene is about −0·7; it becomes more negative at lower acetylene pressures, but the accuracy is less here, the true initial rates probably being lower than those

TABLE II.

(*a*) Effect of hydrogen pressure on $(-dp/dt)_0$ over Pt-2 at 73° (C_2H_2 pressure = 199—205 mm.).

No. of expt.	7	4	5	14	2	6	12	15	3
H_2 press. (mm.)	54	100	197	200	201	299	299	398	400
$(-dp/dt)_0$ (mm./min.)	0·8	1·4	3·0	3·5	2·6	5·0	5·5	9·0	6·3

(*b*) Effect of C_2H_2 pressure on $(-dp/dt)_0$ over Pt-2 at 73° (H_2 pressure = 298—301 mm.).

No. of expt.	10	13	9	8	6	12	11
C_2H_2 press. (mm.)	52	75	104	153	201	202	303
$(-dp/dt)_0$ (mm./min.)	*ca.* 40	12	8·6	6·7	5·0	5·5	4·4

tabulated. A series of 43 runs over a specimen of Pt-1 at 162° gave very similar results; in this case the order with respect to acetylene was zero at pressures of that gas above *ca.* 150—200 mm. in the presence of 200 mm. of hydrogen, but the negative order extended to higher acetylene pressures when more hydrogen was present.

These data are in harmony with the more qualitative results of Farkas and Farkas (*loc. cit.*), who have already given their general explanation in terms of strengths of adsorption. The tendency towards zero order with respect to acetylene suggests that the adsorption film becomes saturated with respect to that gas when its pressure exceeds a certain value, which increases with the hydrogen pressure. It is possible that some ethane formation is included in the measured initial rate, especially at the lowest acetylene pressures, and therefore the observed orders cannot be identified with certainty with those of the reaction $C_2H_2 + H_2 = C_2H_4$, but since we expect more hydrogen to favour ethane production and more acetylene to discourage it, we see that the maximum order of the above reaction with respect to hydrogen is *ca.* 1·2, and that its order with respect to acetylene will not be more negative than the apparent orders already given.

The values of $-dp/dt$ during reaction (before any acceleration) are in fair harmony with these orders, ethylene and ethane being supposed to have no influence on $-dp/dt$.

The effect of gas pressures on the yields is not large. For instance, at *ca.* 70° over Pt-2 the yield of C_2 hydrocarbons is about 90% with 200 mm. of acetylene and either 200 mm. or 400 mm. of hydrogen. Reaction leading to products other than C_2 hydrocarbons (reaction II) therefore seems to resemble the simple hydrogenation (reaction I) in its order with respect to hydrogen. A slow increase in yield of C_2 products with hydrogen : acetylene ratio may occur, however, and an increase of this type is indicated by the results of previous workers (see above).

(iv) *Effect of Temperature.*—Table III shows results with 2 : 1 hydrogen : acetylene mixtures over Pt-2 (t_{170} = time in mins. required for Δp to reach 170 mm.). Catalyst activity varied somewhat, but the plot of $\log_{10} t_{170}$ against $1000/T$ (T = absolute temperature) is a reasonably straight line of slope 3·0 with respect to the $1000/T$ axis. With $\log_{10} (-dp/dt)_0$ against $1000/T$ the corresponding slope is *ca.* − 2·6, the points being rather more scattered. During each run, $-dp/dt$ decreased slightly.

The ethylene : ethane ratio is increased by a rise and lowered by a fall in temperature; lower temperatures therefore favour ethane production in the early stages.

To determine the activation energy of $C_2H_2 + H_2 = C_2H_4$ it is necessary to know whether any ethane formation contributes to the measured initial rate, and, if so, how its contribution varies with temperature. If we assume a contribution independent of temperature (the contribution, if any, is probably small in the initial reaction) we have :

$$\frac{d \log_{10} (d[C_2H_4]/dt)_0}{d(1000/T)} = \frac{d \log_{10} (-dp/dt)_0}{d(1000/T)} \approx -2{\cdot}6$$

since the yield of C_2 hydrocarbons varies little with temperature. A variation in initial ethylene/ethane ratio

TABLE III.

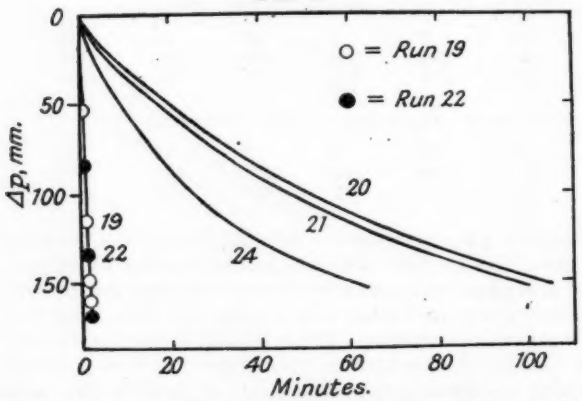
Effect of temperature.

(Acetylene admitted first; $\Delta p = 170$ mm.; the products contained 0—3 mm. of unsaturated hydrocarbons higher than C_2.)

Expt. no.	Temp.	Initial press. (mm.). C_2H_2.	Initial press. (mm.). H_2.	$(-dp/dt)_0$, mm./min.	t_{170}.	Press. (mm.) in gaseous product. C_2H_2.	C_2H_4.	H_2.	C_2H_6.	Yield (%). C_2H_4.	Yield (%). C_2H_6.	Ratio C_2H_4/C_2H_6.
2	16±1°	201	404	0·05	4130	93	56	240	44	52	41	1·27
3	74	201	404	4·0	38	89	60	240	37	54	33	1·62
4	18±2	200	400	0·27	2520	96	46	235	48	44	46	0·96
5	87	200	404	6·5	27·7	89	59	240	37	53	33	1·60
6	2±2	199	402	0·014	16110	91	48	233	49	45	45	1·0
7	101	199	405	12·0	16	84	62	239	34	54	30	1·8
8	56	199	403	0·8	320	—	—	—	—	—	—	—
9	120	199	390	18·0	9	79	71	232	31	59	26	2·26

sufficient to make the above expression inapplicable is very unlikely. The energy of activation of $C_2H_2 + H_2 = C_2H_4$ is therefore about 12 kg.-cals.; Farkas and Farkas (*loc. cit.*) found 12—17 kg.-cals.

FIG. 5.



Initial pressures (in order of admission): runs 19 *and* 22, 196—200 *mm.* C_2H_4, 200 *mm.* H_2; *run* 20, 201 *mm.* C_2H_2, 202 *mm.* H_2; *run* 21, 202 *mm.* C_2H_2, 200 *mm.* C_2H_4, 203 *mm.* H_2; *run* 24, 202 *mm.* C_2H_2, 199 *mm.* O_2, 199 *mm.* H_2.

The total yield of C_2 products appears a little lower at 74—120° (84—87%) than at 0—20° (90—93%); this suggests that reaction (II) has a heat of activation of roughly 1—2 kg.-cals. higher than that of $C_2H_2 + H_2 = C_2H_4$. This is qualitatively in harmony with results of previous workers and with the lower yields of C_2 products over Pt-1 at 145° and 163°.

(v) *Effects of Ethylene and Oxygen.*—Fig. 5 shows the influence of these gases, the Pt-2 catalyst being that used in (iii). Ethylene hydrogenation (run 19) was much more rapid than the acetylene–hydrogen reaction at the same pressures (run 20). With ethylene, acetylene, and hydrogen present (run 21) dp/dt was almost the same as when the ethylene was omitted (run 20), though run 22 (ethylene hydrogenation) showed that the activity of the catalyst had fallen very little. After deduction of the initial ethylene in run 21, the products (Δp = 154 mm.) were almost the same as in run 20 (yields: run 20, ethylene 58, ethane 30%; run 21, ethylene 49, ethane 36%). The ethane yield in run 21 is thus raised only slightly by the added ethylene, which therefore acts principally as a diluent, in harmony with the deduced adsorption relationships.

Addition of oxygen (run 24) increased $-dp/dt$ somewhat, and an abnormally large removal of hydrogen as products other than C_2 hydrocarbons occurred. If 40 mm. of water vapour are assumed to be formed (Δp = 154 mm.), the final pressures are: C_2H_2, 114; C_2H_4, 39; H_2, 38; C_2H_6, 28; O_2, 172; CO and CO_2, each *ca.* 3 mm. (yields: ethylene 45, ethane 32%). The 27 mm. of oxygen removed are accounted for within error as water and oxides of carbon. The simultaneous acetylene–hydrogen reaction appears to be largely unaltered, though the yields of C_2 products are possibly lowered slightly. This is the simplest explanation of the analytical data. It is noteworthy that oxidation (chiefly of hydrogen) can occur without retarding the acetylene–hydrogen reaction; this, and the failure of oxygen to raise the yield of C_2 products, distinguish the effect of that gas over platinum from that observed with nickel catalysts (Part III).

(vi) *General Discussion.*—Except for the above effects of oxygen upon it, the reaction over platinum has a close qualitative resemblance to that over nickel. Thus two types of reaction, (I) and (II), occur at temperatures and acetylene pressures at which acetylene alone undergoes virtually no change over the same catalysts. Reaction (II) leads to hydrocarbons of roughly the same mean molecular weight as the corresponding products over nickel, though the structures formed over platinum remain to be determined. The reaction orders indicate strong adsorption of acetylene and weak adsorption of hydrogen on both metals, and the heats of activation are also similar over both. The differences between the kinetics and heats of activation of reactions (I) and (II) are of the same type over platinum as over nickel. Unknown factors cause a greater yield of C_2 products over platinum, but the general phenomena strongly suggest that similar mechanisms of reaction operate over platinum and nickel (and probably other catalysts; see Part II).

The early production of ethane on platinum shows that some ethylene is present in the adsorption film, despite the stronger adsorption of acetylene. This may be a result of direct competition between acetylene and ethylene for sites which can adsorb either, but it is possible that parts of the surface can adsorb ethylene

but not acetylene [*e.g.*, perhaps the (111) crystal face; cf. Herington, *Trans. Faraday Soc.*, 1941, **37**, 361], and that at such sites hydrogenation of ethylene can continue relatively slowly, ethylene being displaced by acetylene from the sites where ethane is formed most rapidly in the absence of acetylene. Alternatively, ethylene when formed may remain long enough on the metal to have a chance of being hydrogenated further before desorption: the increase in ethane formation at higher hydrogen pressures perhaps suggests that this effect is operative.

The catalytic metal influences the selectiveness of ethylene production. For instance, previous workers have claimed that palladium causes more selective ethylene production than platinum (Paal and Schwarz, *loc. cit.*; Paal and Hohenegger, *Ber.*, 1915, **48**, 275; Morris and Reyerson, *loc. cit.*), and total selectiveness over palladium was postulated by Cremer, Knorr, and Plieninger (*Z. Elektrochem.*, 1941, **47**, 737). In the present work (Part V, to be published) the more selective action of palladium than of platinum has been confirmed, and the case of acetylene thus falls into line with many data on catalytic hydrogenation of substituted acetylenes, in which, in general (though the phenomena doubtless depend on the substituents as well as the catalyst), platinum does not promote a truly selective formation of the ethylenic derivative, whereas palladium is more favourable for such selective hydrogenation (*e.g.*, Lebedev and Stern, *J. Gen. Chem. U.S.S.R.*, 1932, **2**, 249; Zal'kind *et al.*, *ibid.*, 1933, **3**, 91, and many other papers; Lebedev, Gulyaeva, and Vasil'ev, *loc. cit.*). In some (but by no means all) such reductions, the rate of hydrogenation increases when the acetylenic substance is almost completely removed. In these cases a stronger adsorption of the triple- than of the double-bonded compound (as with acetylene itself) is indicated, and may well occur even when there is no such increase in rate (cf., *e.g.*, acetylene on nickel, Part I).

At present it is difficult to relate the degrees of selectiveness of hydrogenation of acetylene on various metals to the differences in strengths of adsorption of acetylene and ethylene on those catalysts. For instance, the more selective action of palladium might be related to a weaker adsorption of ethylene by palladium than by, *e.g.*, platinum. Fischer and Knorr's data (*Z. Elektrochem.*, 1937, **43**, 608) indicate that ethylene is not strongly adsorbed on palladium containing hydrogen at room temperature, whereas Farkas and Farkas (*J. Amer. Chem. Soc.*, 1938, **60**, 22) give evidence that, under those conditions, ethylene is strongly adsorbed on platinum. Unfortunately, however, other data (Bruns and Ablezova, *Acta Physicochim. U.R.S.S.*, 1934, **1**, 90) indicate much weaker adsorption of ethylene on platinum, so until more results are available it is premature to ascribe the more selective action of palladium to so simple a cause. We have already seen that other factors than strengths of adsorption (*e.g.*, relative effectiveness of different types of surface sites) may be concerned.

Similarly, though the effect of temperature on the ethylene/ethane ratio over platinum might be related to an increased difference in strengths of adsorption of acetylene and ethylene at higher temperatures, it might also be due to the true activation energy of $C_2H_4 + H_2 = C_2H_6$ being lower than that of $C_2H_2 + H_2 = C_2H_4$ (cf. Farkas and Farkas, *loc. cit.*, 1939).

The author wishes to thank Mr. D. Ll. Hammick for his interest in and advice on the work described in this and the preceding paper, and the Department of Scientific and Industrial Research for a grant.

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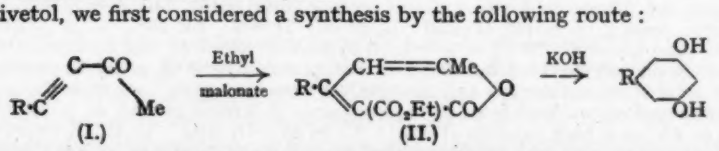
82. *A New Synthesis of Olivetol.*

By R. M. ANKER AND A. H. COOK.

A convenient synthesis of orcinol starting from ethyl crotonate and ethyl acetoacetate is described; a similar series of reactions from methyl Δ^{α}-octenoate provides an improved route to olivetol.

OLIVETOL (5-*n*-amylresorcinol) was first obtained (Asahina and Asano, *Ber.*, 1932, **65**, 475) by degrading the lichen acid, olivetonic acid. This constitution was verified by condensing ethyl *n*-hexoylacetate with ethyl acetonedicarboxylate; the product, presumably ethyl dihydro-olivetoldicarboxylate, was, without isolation, hydrolysed, decarboxylated and apparently oxidised by fusion with alkali. Asahina and Nogami (*Ber.*, 1935, **68**, 1500) described a more rational synthesis *via* 3 : 5-dimethoxyvalerophenone, itself obtained by propylation of the rather difficultly accessible ethyl 3 : 5-dimethoxybenzoylacetate, followed by hydrolysis. Disadvantages were partly overcome (Asahina, *Ber.*, 1936, **69**, 1643) by preparing 3 : 4 : 5-trimethoxyvalerophenone, which is directly reducible with sodium and alcohol to olivetol dimethyl ether. The method of Suter and Weston (*J. Amer. Chem. Soc.*, 1939, **61**, 232) by which dimethoxyvalerophenone is reduced is made tedious by the sulphonation of benzoic acid, alkali fusion, etc.

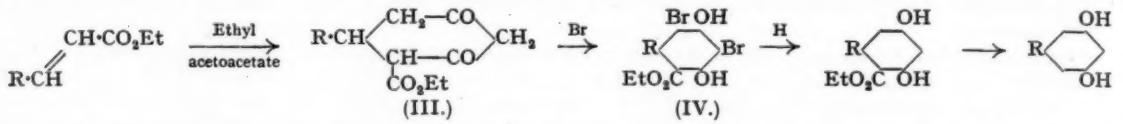
Having need of olivetol, we first considered a synthesis by the following route:



(I.) (II.)

The initial step is comparable with the addition of ethyl malonate to benzoylphenylacetylene (Kohler, *J. Amer. Chem. Soc.*, 1922, **44**, 379) and the second with the conversion of dehydracetic acid into orcinol (Collie

and Myers, J., 1893, **63**, 122). In model experiments hexynyl methyl ketone (I, R = Bu) was submitted to the Michael reaction, and the resulting *lactone* (II, R = Bu) hydrolysed to a product apparently identical with 5-*n*-butylresorcinol but this approach was abandoned because of the relatively difficult accessibility of the required acetylenic ketone. The series (R = Me) does not appear to have been used as a synthesis of orcinol,



(III.) (IV.)

yet each of the individual reactions has been effected at different times. The series does indeed provide a very convenient synthesis of orcinol, particularly when the reduction of the bromo-compound (IV, R = Me) is carried out over palladium on a colloidal carrier (Rampino and Nord, *J. Amer. Chem. Soc.*, 1941, **63**, 2745). Hydrolysis and decarboxylation of (III, R= Me) and oxidation of the resulting dihydro-orcinol were less satisfactory; dihydro-orcinol was not oxidised to orcinol by selenium dioxide in ethanol at 80° and the bromination procedure of Merling (*Annalen*, 1894, **278**, 44) was troublesome as a preparative method. Addition of ethyl acetoacetate to the readily available methyl Δ^{α}-octenoate gave *ethyl dihydro-olivetolcarboxylate* (III, R = C_5H_{11}) in good yield and this was smoothly converted into *ethyl dibromo-olivetolcarboxylate* (IV, R = C_5H_{11}). Reduction of the bromo-ester over palladium on polyvinyl alcohol led to *ethyl olivetolcarboxylate*, which was hydrolysed and decarboxylated in the usual way. The overall yield from the octenoate to olivetol was more than 30% of the theoretical; whereas previous preparations were described as glasses, the present material readily crystallised, though it could only be recrystallised in a solvated form. Its identity was established by its colour reactions and by comparison of its hydrate and tribromo-derivative (Asahina, *loc. cit.*) with those of authentic olivetol which was kindly furnished by Dr. F. Bergel of Roche Products Ltd.

Experimental.

Oct-3-yn-2-one (15 g.) was added to ethyl sodiomalonate prepared from ethanol (20 c.c.), sodium (0·4 g.), and ethyl malonate (19·5 g.), and the red solution heated at 90° for 1 hour. Addition of water (3 vols.) and excess of acetic acid gave the *lactone* (II, R = C_4H_9), which was extracted with chloroform and distilled eventually in a vacuum; it was an oil, b. p. 157°/5 mm. (yield, 17 g. or 50%) (Found: C, 65·4; H, 7·4. $C_{13}H_{18}O_4$ requires C, 65·5; H, 7·6%). Hydrolysis and decarboxylation of the lactone by successive treatment with sodium hydroxide and hydrochloric acid (cf. Kohler, *loc. cit.*), extraction of the acid with chloroform, and fusion for 25 mins. at 250° with a 1 : 1 mixture of sodium and potassium hydroxides, followed by acidification and extraction with chloroform, gave a small quantity of 5-*n*-butylresorcinol, m. p. 79° (lit., m. p. 82°).

Preparation of Orcinol.—Ethyl crotonate (115 g.) was added slowly to a solution prepared from ethanol (300 c.c.) sodium (23 g.), and ethyl acetoacetate (140 g.). After refluxing for 5 hours, the solution was cooled to 0°, and the sodio-compound (180 g. or 82%) collected. Decomposition with acid gave ethyl dihydro-orcinolcarboxylate, which crystallised on standing (yield, 97%) (cf. Schilling and Vorländer, *Annalen*, 1898, **308**, 195). The ester (140 g.) in acetic acid (450 c.c.) was treated with bromine (105 c.c.) in acetic acid at ~40°, and the mixture stirred overnight; ethyl dibromo-orcinolcarboxylate was then collected and recrystallised from ethanol (yield, 195 g. or 80%, a further quantity being obtained from the filtrates and mother-liquor); it had m. p. 144° (cf. Sonn, *Ber.*, 1928, **61**, 926). The bromo-ester (80 g.) in N-sodium hydroxide (700 c.c.) was rapidly hydrogenated over 2% palladium (from 0·5 g. of palladium chloride) on polyvinyl alcohol (Rampino and Nord, *loc. cit.*). Addition of sodium chloride (120 g.) precipitated the catalyst and acidification and extraction with chloroform gave ethyl orcinolcarboxylate, m. p. 132—133° (yield, 35 g. or 80%) (cf. Sonn, *loc. cit.*). The ester (17 g.) was warmed for 2 hours at 90° with sodium hydroxide (40 g.) in water (150 c.c.), and the acidified solution heated to boiling for 3 mins. and cooled. Extraction with ether and distillation gave orcinol (8·6 g. or 80%), m. p. 106—108°, b. p. 147°/5 mm. Its m. p. was not depressed by an authentic specimen and on bromination it gave pentabromo-orcinol, m. p. 125°.

Preparation of Olivetol.—*n*-Hexaldehyde (*Org. Syn.*, 1936, **16**, 41) (150 g.), malonic acid (80 g.), and pyridine (280 g.) were heated at 40—54° for 20 hours, the cooled solution treated with 50% (by vol.) sulphuric acid (220 c.c.), and the Δ^{α}-octenoic acid extracted with ether and distilled. Hexaldehyde (10 g.) was recovered, and Δ^{α}-octenoic acid (160 g. or 75%), $n_D^{20°}$ 1·4588, collected at 102°/5 mm. (cf. Bachmann, *J. Amer. Chem. Soc.*, 1933, **55**, 4281). The acid was converted into its methyl ester, b. p. 97°/18 mm. (yield, 160 g. or 91%) by diazomethane in ether. A boiling solution of ethyl acetoacetate (115 g.) in ethanol (260 c.c.) in which sodium (20 g.) had been dissolved was treated dropwise with methyl Δ^{α}-octenoate (114 g.), and the whole refluxed for 4 hours. The cold product was collected, the filtrate refluxed for a further 5 hours, and, after cooling, a further quantity of sodio-compound collected. The combined precipitates of sodio-compound (180 g.) were dissolved in water (1 l.) and treated with concentrated hydrochloric acid (100 c.c.). Crude *ethyl dihydro-olivetolcarboxylate* (145 g. or 71%) soon solidified and was recrystallised from light petroleum, separating in microscopic prisms, m. p. 64—65° (Found: C, 66·3; H, 8·85. $C_{14}H_{22}O_4$ requires C, 66·15; H, 8·75%). The filtrates from the sodio-compound gave no considerable amount of the desired ester and the yield was depressed under other conditions or by the use of sodamide in toluene. The ester (158 g.) in acetic acid (400 c.c.) was slowly treated, with stirring but without cooling, with bromine (104 c.c.) in acetic acid (400 c.c.), and the solution finally heated at 60° until evolution of hydrogen bromide ceased. Cooling to 0° overnight gave *ethyl dibromo-olivetolcarboxylate*, more being obtained by evaporating the filtrate in a vacuum and cooling (total yield, 140 g. or 55%); it separated from light petroleum in microscopic prisms, m. p. 67° (Found: C, 41·05; H, 4·2; Br, 39·7. $C_{14}H_{18}O_4Br_2$ requires C, 41·0; H, 4·4; Br, 39·0%). The dibromo-ester (70 g.) in N-sodium hydroxide (500 c.c.) was hydrogenated at room temperature and 1 atm. over palladium on polyvinyl alcohol (0·5 g. of $PdCl_2$). Almost 90% of the theoretical quantity of hydrogen was rapidly taken up; *ethyl olivetolcarboxylate* and the catalyst were then salted out from the acidified solution, and the ester extracted with ether and crystallised from light petroleum; it formed prisms, m. p. 69° (yield 34 g. or 80%) and sublimed very slowly at 50° in a high vacuum (Found: C, 66·65; H, 8·05. $C_{14}H_{20}O_4$ requires C, 66·65; H, 8·0%). The crude ester (31 g.) was hydrolysed and decarboxylated by boiling with sodium hydroxide (40 g.) in water (150 c.c.) for 2 hours, acidifying, boiling again for 3 minutes, and extracting with ether. Olivetol prepared by this route (yield, 20·5 g. or 92%) distilled at 145° in a high vacuum and solidified to an almost colourless, crystalline mass, m. p. 49°. It

could be recrystallised from benzene–light petroleum, but separated in solvated form. It gave all the colour reactions of olivetol prepared by other processes (see Asahina and Nogami, *loc. cit.*) and in addition gave a green-brown coloration with ethanolic ferric chloride; on hydration the hydrate, m. p. 40—41°, was obtained, which depressed the m. p. of the unhydrated olivetol. The hydrate was identical with that of authentic olivetol, and the tribromo-compounds, m. p. 84°, prepared from the present material and from authentic olivetol, were identical.

The authors thank Professor I. M. Heilbron, D.S.O., F.R.S., for his interest and encouragement and I.C.I. Ltd (Dyestuffs Division) for grants.

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83. *New Syntheses of Heterocyclic Compounds. Part III. Azaphenoxazines.*

By V. A. PETROW and E. L. REWALD.

The aim of the present investigation was the preparation of analogues of methylene-blue containing nuclear nitrogen in one of the benzenoid rings. Representatives have been obtained in the azaphenoxazine series as exemplified by 7 : 9-*dinitro*-4-, 5-*nitro*-3-, 5 : 9-*dinitro*-3- and 5 : 8-*dinitro*-3-*azaphenoxazines*, and reduced to the corresponding *amino*-compounds. The method was a modification of Turpin's reaction (J., 1891, **59**, 722) and its extension by Misslin and Bau (*Helv. Chim. Acta*, 1919, **2**, 295).

THE value of methylene-blue (I) in the treatment of malaria was first demonstrated by Guttmann and Ehrlich (*Berl. Klin. Woch.*, 1891, **28**, 593) and this compound formed the starting point for extensive antimalarial studies which culminated in the preparation of pamaquin, 8-diethylamino*iso*pentylamino-6-methoxyquinoline. Among the possible alternative variations of the methylene-blue molecule, the one involving the replacement of one of the benzenoid rings by one containing nitrogen (II) seemed from the chemotherapeutic standpoint worthy of exploration. Azaphenthiazines have not, however, hitherto been described in the literature. We have carried out model experiments on the synthesis of the related azaphenoxazines, for which the starting materials are relatively more accessible. The application of our results to the preparation of azaphenthiazines will be reported in a subsequent communication.

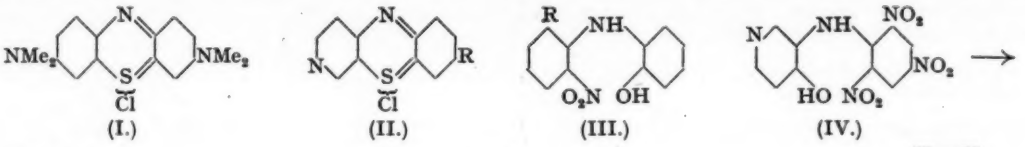
The facile synthesis of dinitrophenoxazine from picryl chloride and *o*-aminophenol in the presence of alkali was discovered by Turpin (J., 1891, **59**, 722) (cf. Kehrmann, *Ber.*, 1899, **32**, 2603). Subsequently the reaction was found to proceed equally readily with 2 : 6-dinitrochlorobenzene (Ullmann, *Annalen*, 1909, **366**, 110) and was ultimately extended to embrace 6-substituted 2-nitrochlorobenzenes *via* the intermediate compounds (III) (Ullmann, *ibid.*, p. 79; G.P. 200,736). The mechanism of the reaction was studied by Brady and Valler (J., 1930, 1218), who found that ring closure of (III) proceeded equally readily when R was either an electropositive or an electronegative substituent. They concluded that the effect of R (formula III) was largely stereochemical, forcing the *o*-nitro-group into close proximity to the hydroxyl group. Scale models confirm this hypothesis.

With the object of orienting the nitration product of 3-hydroxypyridine, to which he assigned the 2-nitro-structure, Plazek (*Rocz. Chem.*, 1936, **16**, 504) applied Turpin's reaction (*loc. cit.*) to the corresponding amino-compound, obtaining a product corresponding on analysis to a 7 : 9-dinitro-5-azaphenoxazine, but no evidence in support of this structure was given. Although this result is of interest, 2-amino-3-hydroxypyridines are so difficultly accessible as to preclude work along these lines. We have attempted to extend the reaction, however, to the readily accessible 3-amino-4-hydroxypyridine (Crowe, J., 1925, **127**, 2029). Numerous experiments were carried out under various conditions, but the products, which were all highly coloured compounds containing halogen, exploded on warming and dissolved in alkalis with the production of intense purple colours. This behaviour is paralleled by the reactions of dinitrophenylpyridinium chloride, the addition compound of chlorodinitrobenzene and pyridine, which undergoes conversion into coloured derivatives of glutaconaldehyde on treatment with alkali (Zincke, *Annalen*, 1904, **330**, 361). Similar results were obtained with the analogous 3-amino-4-hydroxyquinaldine of Conrad and Limpach (*Ber.*, 1887, **20**, 950). We were thus forced to conclude that the picryl chloride reacted preferentially with the ring nitrogen and not with the 3-amino-group. It may be mentioned in this connection that Lawson, Perkin, and Robinson (J., 1924, **125**, 628) were unable to condense substituted 3-aminoquinolines with chloronitrobenzenes.

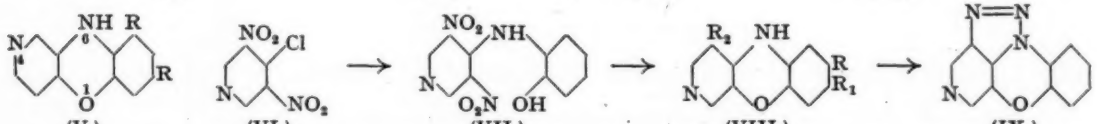
We succeeded ultimately in preparing an azaphenoxazine from 3-amino-4-hydroxypyridine by employing the modification of Turpin's reaction (*loc. cit.*) described by Misslin and Bau (*Helv. Chim. Acta*, 1919, **2**, 295), who replaced picryl chloride by 2 : 4 : 6-trinitroanisole. When approximately equimolecular quantities of the components were heated in methyl-alcoholic solution, the sparingly soluble 3-*picrylamino*-4-*hydroxypyridine* (IV) separated. This compound passed smoothly on warming with one molecule of potassium hydroxide into 7 : 9-*dinitro*-4-*azaphenoxazine* (V; R = NO_2) with simultaneous production of nitrite. Reduction with stannous chloride gave an unstable diamino-compound (V; R = NH_2), isolated as the *trihydrochloride*.

We next turned our attention to the reverse procedure, *viz.*, the condensation of a pyridine analogue of 2 : 6-dinitrochlorobenzene with *o*-aminophenol (cf. Ullmann, *loc. cit.*). 3 : 5-Dinitro-4-hydroxypyridine (Crowe, *loc. cit.*) on treatment with phosphorus pentachloride at 170° was converted into 4-*chloro*-3 : 5-*dinitropyridine* (VI), a compound so susceptible to hydrolysis that it was found desirable to employ it *in situ*. On treating (VI) with *o*-aminophenol in the presence of sodium acetate, *dinitropyridyl*-*o*-*aminophenol* (VII) was

obtained, smoothly cyclised to *5-nitro-3-azaphenoxazine* (VIII; R = R_1 = H, R_2 = NO_2) by alkalis or aqueous ammonia, with simultaneous formation of nitrite. Ring closure also took place when the intermediate com-



(I.) (II.) (III.) (IV.)



(V.) (VI.) (VII.) (VIII.) (IX.)

pound (VII) was heated in alcoholic solution with a few drops of piperidine or other secondary base, oxides of nitrogen being evolved. Reduction gave *5-amino-3-azaphenoxazine* (VIII; R = R_1 = H, R_2 = NH_2), characterised by a *monoacetyl* derivative. Treatment of this amino-base with nitrous acid gave the *diazole* (IX). This behaviour is characteristic of an *o*-aminodiphenylamine. It is shown by such structurally analogous compounds as 9-amino-5 : 10-dihydroacridine (Clemo, Perkin, and Robinson, J., 1924, **125**, 1754) and 1 : 3-diaminophenthiazonium chloride (Kehrmann and Steinberg, *Ber.*, 1911, **44**, 3015) and is strong evidence in support of the formulations assigned to our products.

Nitration of 5-nitro-3-azaphenoxazine in glacial acetic acid gave a *dinitro*-derivative. By analogy with the nitration of phenoxazine (Kehrmann and Saager, *Ber.*, 1903, **36**, 478) it was expected that the entrant nitro-group would be introduced in position R_1 (formula VIII) or less probably R. Its formulation as 5 : 9-*dinitro*-3-*azaphenoxazine* (VIII; R_1 = R_2 = NO_2, R = H) followed from the synthesis of a compound of this structure from 4-chloro-3 : 5-dinitropyridine and 5-nitro-*o*-aminophenol, identical in every respect with the product of direct nitration. 5 : 8-*Dinitro*-3-*azaphenoxazine* (VIII; R = R_2 = NO_2, R_1 = H) was similarly prepared from 4-nitro-*o*-aminophenol.

Reduction of these dinitro-compounds gave the corresponding 5 : 9-*diamino*-3-*azaphenoxazine* (VIII; R_1 = R_2 = NH_2, R = H) and 5 : 8-diamino-3-azaphenoxazine (VIII; R = R_2 = NH_2, R_1 = H), isolated as the *dihydrochlorides*. The free *base* from the 5 : 9-isomeride proved very susceptible to oxidation, rapidly darkening on exposure to air or on liberation from its salts with sodium hydroxide. All attempts to oxidise it to a well-defined quinonoidal form, however, proved unsuccessful.

The results of the pharmacological tests on some of the above compounds will be published elsewhere.

Experimental.

M. p.'s are corrected. Microanalyses are by Mr. R. Maxim, University Chemical Laboratory, Cambridge, and The Wellcome Chemical Works, Dartford, Kent.

3-Picrylamino-4-hydroxypyridine (IV).—3-Nitro-4-hydroxypyridine (5 g.) (Crowe, *loc. cit.*), reduced iron (15 g.), and anhydrous calcium chloride (1 g.) were heated under reflux in 80% methanol (125 ml.) for 90 minutes, the iron residues collected and extracted with a further quantity of boiling methanol (50 ml.), and the combined filtrates treated with trinitroanisole (5 g.; 0·6 mol.) (Brady and Horton, J., 1925, **127**, 2232). After 30 minutes' refluxing, *3-picrylamino-4-hydroxypyridine* separated; it formed golden-yellow platelets from aqueous acetic acid, m. p. 201° (decomp.) (Found: C, 41·3; H, 2·5; N, 22·0. $C_{11}H_7O_7N_5$ requires C, 41·1; H, 2·2; N, 21·8%). Yield, 5 g. (80%).

7 : 9-Dinitro-4-azaphenoxazine (V; R = NO_2).—To 3-picrylamino-4-hydroxypyridine (10 g.), suspended in spirit (200 ml.), potassium hydroxide (2 g.; 1·1 mols.) was added, the mixture refluxed for 2 hours, and the product collected after cooling. 7 : 9-*Dinitro*-4-*azaphenoxazine* formed red needles from alcoholic acetic acid, m. p. 229—230° (Found: C, 47·9; H, 2·3; N, 20·1. $C_{11}H_5O_5N_4$ requires C, 48·2; H, 2·2; N, 20·4%). Yield, 6 g. (70%). The filtrate was evaporated to dryness; an aqueous extract of the residue gave positive nitrite tests with the Griess–Ilosvay reagent, dilute acid, etc.

7 : 9-Diamino-4-azaphenoxazine Trihydrochloride (V; R = NH_2,HCl).—The corresponding dinitro-compound (2 g.), suspended in concentrated hydrochloric acid (15 ml.), was treated with stannous chloride (10 g.) in concentrated hydrochloric acid (15 ml.). After being heated for 1 hour on the water-bath, the mixture was diluted with water (1 l.), and the tin removed as sulphide. The filtrate, on concentration under reduced pressure on the water-bath to *ca.* 10 ml., deposited pale yellow needles of *7 : 9-diamino-4-azaphenoxazine trihydrochloride*, m. p. above 300° (Found: Cl, 33·4. $C_{11}H_{10}ON_4$,3HCl requires Cl, 32·9%). Yield, 20—25%. The compound was very susceptible to oxidation, undergoing partial decomposition when attempts were made to recrystallise it from a variety of solvents. Attempts to isolate the free base were unsuccessful, rapid oxidation taking place.

4-Chloro-3 : 5-dinitropyridine (VI).—3 : 5-Dinitro-4-hydroxypyridine (10 g.) (Crowe, *loc. cit.*) was treated under reflux with phosphorus pentachloride (18 g.; 1·2 mols.) and a little phosphorus oxychloride at 160—170° for 1 hour. After removal of the phosphorus halides under reduced pressure on the water-bath the residue was extracted with boiling light petroleum (b. p. 80—100°). *4-Chloro-3 : 5-dinitropyridine*, which separated on cooling, formed colourless needles from light petroleum, m. p. *ca.* 240° (decomp.) (with preliminary softening at *ca.* 60°) (Found: Cl, 17·1. $C_5H_2O_4N_3Cl$ requires Cl, 17·4%). The compound rapidly decomposes on keeping, reverting to the dinitrohydroxypyridine.

Dinitropyridyl-o-aminophenol (VII).—3 : 5-Dinitro-4-hydroxypyridine (10 g.) was chlorinated as described above, and the phosphorus halides removed. The residue was treated *in situ* with anhydrous sodium acetate (10 g.), followed immediately by a solution of *o*-aminophenol (6 g.; 1 mol.) in spirit. The mixture was refluxed for 30 minutes, an equal volume of water added, and the product collected after cooling. *Dinitropyridyl-o-aminophenol* formed orange platelets from alcohol (charcoal), m. p. 195° (decomp.) (Found: C, 47·9; H, 2·9; N, 20·2. $C_{11}H_6O_5N_4$ requires C, 47·8; H, 2·9; N, 20·3%). Yield, 9·3 g. (60%).

5-Nitro-3-azaphenoxazine (VIII; R = R_1 = H, R_2 = NO_2).—Crude dinitropyridyl-*o*-aminophenol (9·3 g.), suspended in alcohol, was heated with excess of aqueous ammonia (*d* 0·880) for 15 minutes on the water-bath; after cooling, the solid was collected. *5-Nitro-3-azaphenoxazine* separated from aqueous acetic acid in deep red crystals, m. p. 209—210° (Found: C, 57·6; H, 3·0; N, 18·3. $C_{11}H_7O_3N_3$ requires C, 57·6; H, 3·1; N, 18·3%). Yield, 5·5 g. (70%). The mother-liquors gave positive tests for nitrite (see above).

5-Amino-3-azaphenoxazine (VIII; R = R_1 = H, R_2 = NH_2).—Finely powdered 5-nitro-3-azaphenoxazine (2·5 g.), suspended in alcohol (25 ml.), was treated with stannous chloride (10 g.) in concentrated hydrochloric acid (25 ml.) under reflux until the original red substance had been completely replaced by brown needles; after cooling, the product was collected. *5-Amino-3-azaphenoxazine hydrochloride* formed bright yellow needles from water (charcoal), m. p. above 300° (Found: C, 56·1, H, 4·4; N, 18·3; Cl, 15·6. $C_{11}H_9ON_3$,HCl requires C, 56·1; H, 4·3; N, 17·8; Cl, 15·1%). Yield, 2 g. (80%). *5-Amino-3-azaphenoxazine*, precipitated from a solution of the hydrochloride with ammonia, separated from water (charcoal) in white crystals, m. p. 258—259° (Found: C, 66·0; H, 4·6; N, 21·3. $C_{11}H_9ON_3$ requires C, 66·3; H, 4·5; N, 21·1%). Yield, nearly quantitative. The free base could be obtained in 75% yield directly from the nitro-compound by reduction with reduced iron in aqueous alcohol. When 5-amino-3-azaphenoxazine hydrochloride (2·7 g.) was heated under reflux for 30 minutes with acetic anhydride (40 ml.) and sufficient anhydrous sodium acetate to bring the yellow suspension into solution, *5-acetamido-3-azaphenoxazine* was obtained; it separated from spirit (charcoal) in felted white needles, m. p. 288—289° (decomp.) (Found: C, 64·9; H, 4·6; N, 17·4. $C_{13}H_{11}O_2N_3$ requires C, 64·7; H, 4·6; N, 17·4%).

3-Azaphenoxazine-5 : 6-diazole (IX).—A solution of 5-amino-3-azaphenoxazine hydrochloride (5 g.) in water (15 ml.) and concentrated hydrochloric acid (15 ml.) was cooled to 0°, and an aqueous solution of sodium nitrite (1·5 g.) added dropwise with mechanical stirring. After 1 hour the mixture was heated to boiling; a sparingly soluble hydrochloride then separated. The mixture was cooled, the product collected, and the free base liberated with aqueous ammonia. *3-Azaphenoxazine-5 : 6-diazole* formed white needles from spirit, m. p. 171° (decomp.) Found: C, 63·0; H, 2·7; N, 26·7. $C_{11}H_6ON_4$ requires C, 62·9; H, 2·9; N, 26·7%).

5 : 9-Dinitro-3-azaphenoxazine (VIII; R_1 = R_2 = NO_2, R = H).—(a) Finely powdered 5-nitro-3-azaphenoxazine (2·2 g.) was suspended in glacial acetic acid (16 ml.), and fuming nitric acid (*d* 1·5) (5 ml.) added dropwise with mechanical stirring at 0° during 15 minutes. The bright red product was collected, washed with glacial acetic acid, and crystallised from nitrobenzene (charcoal), yielding bright red crystals of *5 : 9-dinitro-3-azaphenoxazine*, m. p. 312° (decomp.) (Found: C, 48·5; H, 2·3; N, 20·6. $C_{11}H_5O_5N_4$ requires C, 48·2; H, 2·2; N, 20·4%). A further small quantity of material was obtained by partial neutralisation of the acid mother-liquors with aqueous ammonia. Yield, 2·4 g. (90%).

(b) Crude 4-chloro-3 : 5-dinitropyridine (prepared from 10 g. of 3 : 5-dinitro-4-hydroxypyridine) was treated with anhydrous sodium acetate (10 g.), followed immediately by an alcoholic solution of 5-nitro-2-aminophenol (8 g.) (Hewitt and King, J., 1926, 882). The mixture was heated under reflux for 15 minutes, and then cooled after addition of sufficient water to produce a turbidity. The product was collected (12 g.; m. p. 220—230°), suspended in alcohol, and heated under reflux with excess of aqueous ammonia (*d* 0·880) for 15 minutes. The product, crystallised from nitrobenzene (charcoal), gave red crystals of *5 : 9-dinitro-3-azaphenoxazine*, m. p. 316° (decomp.) (Found: C, 48·6; H, 2·3; N, 20·6%), not depressed by the compound obtained in (a). Yield, 5 g. (35%).

5 : 8-Dinitro-3-azaphenoxazine (VIII; R = R_2 = NO_2, R_1 = H).—Prepared from 4-nitro-2-aminophenol (Hewitt and King, *loc. cit.*) by the method described in the previous preparation, this formed orange crystals from nitrobenzene, m. p. 318° (Found: C, 48·4; H, 2·2; N, 20·3. $C_{11}H_5O_5N_4$ requires C, 48·2; H, 2·2; N, 20·4%). Yield, 35%. In admixture with the 5 : 9-dinitro-compound a m. p. depression of 40° was obtained

5 : 9-Diamino-3-azaphenoxazine (VIII; R = R_1 = NH_2, R_2 = H).—5 : 9-Dinitro-3-azaphenoxazine (2 g.), reduced iron (8 g.), and anhydrous calcium chloride (0·5 g.) were heated under reflux in 70% alcohol (30 ml.) for 2 hours. After addition of charcoal and a further few minutes' heating the liquid was filtered. White needles of *5 : 9-diamino-3-azaphenoxazine* separated on cooling, m. p. *ca.* 270° (decomp.) (Found: C, 62·4; H, 4·7; N, 26·0. $C_{11}H_{10}ON_4$ requires C, 61·7; H, 4·7; N, 26·2%). Attempts at recrystallisation led to severe discoloration. The *dihydrochloride* formed yellow-green needles from hydrochloric acid, m. p. above 300° (Found: Cl, 24·6. $C_{11}H_{10}ON_4$,2HCl requires Cl, 24·7%). *5 : 9-Diacetamido-3-azaphenoxazine*, prepared by heating the base with 20 vols. of acetic anhydride under reflux for 1 hour, separated from alcohol as the *monohydrate* (Found: loss on drying, 6·2. $C_{15}H_{14}O_3N_4$,H_2O requires H_2O, 5·7%). The anhydrous compound formed lemon-yellow crystals, m. p. above 300° (Found: C, 60·6; H, 4·4; N, 18·6. $C_{15}H_{14}O_3N_4$ requires C, 60·4; H, 4·7; N, 18·8%).

5 : 8-Diamino-3-azaphenoxazine dihydrochloride (VIII; R = R_2 = NH_2,HCl, R_1 = H), prepared as described for the 5 : 9-isomeride, separated from water in yellow needles, m. p. above 300° (Found: Cl, 24·7. $C_{11}H_{10}ON_4$,2HCl requires Cl, 24·7%).

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c/o THE UNIVERSITY CHEMICAL LABORATORIES, CAMBRIDGE.

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84. *Search for New Analgesics. Part I. Homologues of Pethidine and Related Compounds.*

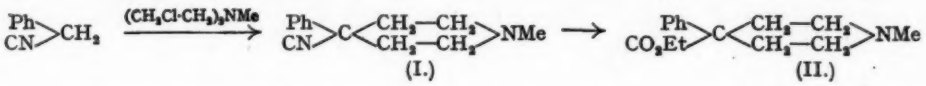
By E. WALTON and (in part) M. B. GREEN.

αα-Bis-(β′-bromoethyl)phenylacetic ester (IV) has been found to react with primary amines to give a series of pethidine *analogues* (V). With ammonia it reacted exceptionally to give *3-(β-aminoethyl)-3-phenyl-2-pyrrolidone* (IX; R = H).

α-(β′-Bromoethyl)-α-phenylbutyrolactone (VII; X = Br) reacted with amines in two ways. With ammonia, the lower primary amines, and secondary amines, it gave aminoethyl lactones (VIII), but with higher primary amines, pyrrolidones (VI) were formed.

THE analgesic drug, pethidine (II), was first synthesised by Eisleb (*Ber.*, 1941, **74**, 1433), by condensing phenyl-

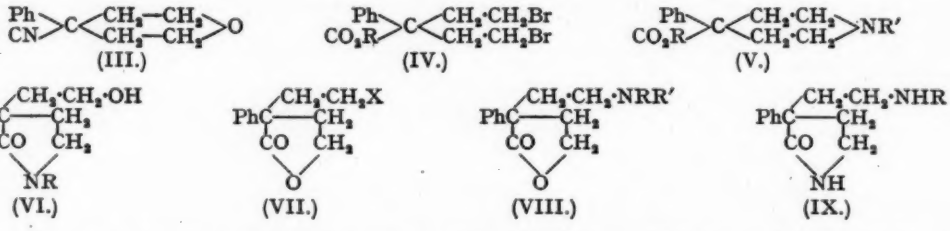
acetonitrile with bis-(β-chloroethyl)methylamine to give 4-phenyl-1-methylpiperidine-4-nitrile (I), which was then converted into the corresponding ethyl ester :—



(I.) (II.)

Probably the main disadvantage of this process lies in the use of the powerful vesicant bis-(β-chloroethyl)-methylamine.

The original object of this research was therefore an alternative synthesis of pethidine avoiding the use of the vesicant, and this was eventually achieved by converting 4-cyano-4-phenylpentamethylene oxide (III) (Eisleb, *loc. cit.*) into αα-bis-(β′-bromoethyl)phenylacetic acid (IV; R = H) and treating the ethyl ester of the latter with methylamine. As this method has recently been recorded by Bergel, Morrison, and Rinderknecht (J., 1944, 267), it is unnecessary to describe it further here. The reactions of the dibromo-acid (IV; R = H) and its immediate derivatives have, however, been more extensively studied by us, with a view to the synthesis of homologues of pethidine and related compounds.



(III.) (IV.) (V.)

(VI.) (VII.) (VIII.) (IX.)

The acid (IV; R = H), on attempted distillation or treatment with dilute alkali, gave good yields of α-(β′-bromoethyl)-α-phenylbutyrolactone (VII; X = Br), which on stronger hydrolysis formed α-(β′-hydroxyethyl)-α-phenylbutyrolactone (VII; X = OH) (compare Bergel *et al., loc. cit.*). Esterification with either diazomethane or diazoethane, however, stabilised the molecule sufficiently for further synthetic work.

Both the ester (IV; R = Et) and the bromo-lactone (VII; X = Br) have now been found to give a series of derivatives on treatment with amines. With ammonia, the ester (IV) gave neither norpethidine (V; R = Et, R′ = H) as expected nor its amide, but 3-(β-*aminoethyl*)-3-*phenyl*-2-*pyrrolidone* (IX; R = H), the structure of which was confirmed by *N*-methylation to 3-(β-methylaminoethyl)-3-phenyl-2-pyrrolidone (IX; R = Me) and by conversion with nitrous acid into α-(β′-hydroxyethyl)-α-phenylbutyrolactone (VII; X = OH). With the primary amines, ethylamine, *n*-propylamine, *n*-butylamine and benzylamine, however, (IV) reacted normally to give a series of pethidine homologues (V), together with smaller amounts of the corresponding lactones (VIII) or lactams (VI), but with aniline only 1 : 3-*diphenyl*-3-(β-*hydroxyethyl*)-2-*pyrrolidone* (VI; R = Ph) was obtained. Attempts to prepare open-chain bis-(dialkylamino)-compounds from (IV) have so far been unsuccessful.

The bromo-lactone (VII; X = Br) with amines formed two distinct types of products. With ammonia, methylamine, ethylamine, and the secondary amines diethylamine, piperidine, methylaniline, and benzylmethylamine, it gave a series of *aminoethyl lactones* (VIII), whereas with the higher primary amines *n*-butylamine, aniline, benzylamine and *cyclo*hexylamine, it yielded feebly basic *hydroxyethyl lactams* of type (VI). With *n*-propylamine both α-(β′-*n*-propylaminoethyl)-α-phenylbutyrolactone (VIII; R = n-C_3H_7, R′ = H) and 3-*phenyl*-3-(β-*hydroxyethyl*)-1-n-*propyl*-2-*pyrrolidone* (VI; R = n-C_3H_7) were formed.

These lactones and lactams showed varying tendencies towards interconversion. Thus α-(β′-aminoethyl)-α-phenylbutyrolactone (VIII; R = R′ = H) existed only in the form of its *hydrochloride*, for with alkali the latter gave the feebly basic 3-(β-*hydroxyethyl*)-3-*phenyl*-2-*pyrrolidone* (VI; R = H), which required excess of acid for reconversion into the neutral hydrochloride of (VIII).

α-(β-Methylaminoethyl)-α-phenylbutyrolactone (VIII; R = Me, R′ = H) was more stable. Its *hydrochloride* yielded the corresponding base on neutralisation, and a crystalline *derivative*, m. p. 151°, with *p*-nitrobenzoyl chloride. On the other hand, preliminary heating of the hydrochloride led to the rapid evolution of hydrogen chloride and the formation of a feebly basic oil, probably 3-phenyl-1-methyl-3-(β-hydroxyethyl)-2-pyrrolidone (VI; R = Me), which gave a p-*nitrobenzoyl* derivative melting at 110—112°.

The *hydrochlorides* of both α-(β′-ethylaminoethyl)-α-phenylbutyrolactone (VIII; R = Et, R′ = H) and α-(β′-*n*-propylaminoethyl)-α-phenylbutyrolactone (VIII; R = n-C_3H_7, R′ = H) also evolved hydrogen chloride on heating to give feebly basic oils (VI ?), but crystalline *p*-nitrobenzoyl derivatives could not be obtained in these cases. Some preliminary attempts to reconvert these crude hydroxyethyl lactams into the corresponding lactones were also unsuccessful.

Several of the compounds described in this paper have been tested for spasmolytic and analgesic activity by Mr. R. H. Thorp at the Wellcome Physiological Research Laboratories, Beckenham, and although spasmolytic activity is still retained to a certain extent in most of these compounds, analgesic activity has been completely abolished. Detailed results will be published elsewhere.

Experimental.

αα-Bis-(β′-bromoethyl)phenylacetic Acid (IV; R = H).—4-Cyano-4-phenylpentamethylene oxide (7·6 g.) was heated with fuming hydrobromic acid (*d* 1·81) (60 ml.) in a sealed tube at 100° for 7 hours. When cold, the resulting brown crystalline mass was washed with water and crystallised from petrol (b. p. 80—100°) (500 ml.), forming needles, m. p. 118° (Found: C, 41·4; H, 4·0; Br, 45·4. Calc. for $C_{12}H_{14}O_2Br_2$: C, 41·2; H, 4·0; Br, 45·7%).

α-(β′-Bromoethyl)-α-phenylbutyrolactone (VII; X = Br).—This was readily prepared from the corresponding acid (IV; R = H) by straight distillation. After melting, the acid (7 g.) evolved hydrogen bromide to give the lactone (4·1 g.), b. p. 204—210°/13 mm. (Found: C, 53·1; H, 4·9; Br, 29·9. Calc. for $C_{12}H_{13}O_2Br$: C, 53·5; H, 4·9; Br, 29·7%). Treatment of the dibromo-acid with cold alkali or even warm water yielded the same lactone.

α-(β′-Hydroxyethyl)-α-phenylbutyrolactone (VII; X = OH).—The bromo-lactone (VII; X = Br) (10 g.) was warmed with *N*-methyl-alcoholic potassium hydroxide (100 ml.) for 1 minute; the oil then went into solution and potassium bromide separated. The filtrate was evaporated to remove alcohol, diluted with water, and washed with ether. The aqueous portion, probably consisting of a solution of potassium αα-bis-(β′-hydroxyethyl)phenylacetate,* was acidified and extracted with ether. The dried ethereal extract on distillation yielded the hydroxy-lactone as a colourless oil, b. p. 220°/15 mm., slightly soluble in hot water (Found: C, 70·6; H, 7·2. Calc. for $C_{12}H_{14}O_3$: C, 69·9; H, 6·8%). The p-*nitrobenzoate* formed tablets, m. p. 116—117° (Found: N, 4·4. $C_{19}H_{17}O_6N$ requires N, 4·0%).

Methyl and ethyl αα-bis-(β′-bromoethyl)phenylacetates (IV; R = Me and Et) were formed by esterification of the corresponding acid with a slight excess of an ethereal solution of diazomethane and diazoethane respectively. On removal of the ether, they were obtained as oils, which readily decomposed into the lactone (VII; X = Br) on heating.

3-*(β-Aminoethyl)-3-phenyl-2-pyrrolidone* (IX; R = H).—The crude ethyl ester (IV; R = Et) (10 g.) and ethyl-alcoholic ammonia (40 ml.) were heated under pressure at 95° for 3 hours. After removal of the alcohol and ammonia, the residue was filtered from ammonium bromide (which was washed with acetone), basified with dilute caustic soda solution, and well extracted with ether or chloroform. The extract, after removal of solvent, crystallised from benzene in tablets (2·4 g.), m. p. 113—114°, very soluble in hot water, but crystallisable from dilute caustic soda solution (Found: C, 70·1; H, 7·9; N, 13·7. $C_{12}H_{16}ON_2$ requires C, 70·6; H, 7·8; N, 13·8%). The *pyrrolidone* tended to absorb carbon dioxide on exposure.

The *hydrochloride* crystallised from alcohol–ether in rectangular plates, m. p. 150—153° (Found: C, 59·6; H, 7·1; N, 11·8; Cl, 14·9. $C_{12}H_{16}ON_2,HCl$, requires C, 59·8; H, 7·1; N, 11·6; Cl, 14·8%). Treatment of an aqueous solution of the hydrochloride with an excess of sodium nitrite and hydrochloric acid yielded an oil, which was extracted with ether and treated with *p*-nitrobenzoyl chloride. A crystalline *p*-nitrobenzoate, m. p. 113—116°, was formed, identical with that obtained from the hydroxy-lactone (VII; X = OH) (*q.v.*).

3-*(β-Methylaminoethyl)-3-phenyl-2-pyrrolidone* (IX; R = Me).—A mixture of the pyrrolidone (IX; R = H) (0·5 g.), methyl iodide (0·4 g.), and sodium carbonate (0·15 g.) in alcohol (3 ml.) was refluxed for 5 minutes. The residue, after removal of the volatile constituents, was made strongly alkaline and extracted with chloroform. The oily extract formed a *hydrochloride*, which crystallised from alcohol–ether in feathery needles, m. p. 177—178° (Found: C, 61·3; H, 7·5; N, 10·6; Cl, 14·1. $C_{13}H_{18}ON_2,HCl$ requires C, 61·3; H, 7·5; N, 11·0; Cl, 14·0%).

Methyl and Ethyl 4-Phenyl-1-methylpiperidine-4-carboxylates (V; R = Me and Et, R′ = Me).—The methyl ester (IV; R = Me) (10 g.) and 27% w/v methyl-alcoholic methylamine (50 ml.) were heated in a sealed tube at 120—130° for 3 hours. The methyl alcohol was removed, and the residue made strongly alkaline with caustic soda and extracted with ether. The extract on distillation gave a lower fraction, b. p. 185—210°/16 mm., which, on treatment with hydrochloric acid, yielded methyl 4-phenyl-1-methylpiperidine-4-carboxylate hydrochloride, crystallising from acetone in prisms (1 g.), m. p. 201—202°, identical with that obtained by Eisleb's method (B.P. 501,135).

The corresponding ethyl ester (pethidine) was obtained in a similar manner but in better yield as a lower fraction, b. p. 175—180°/14 mm. (cf. Bergel *et al.*, *loc. cit.*).

4-Phenyl-1-methylpiperidine-4-carboxyamide was prepared from the corresponding acid chloride by established methods (B.P. 501,135) for comparison with the isomeric 3-(β-methylaminoethyl)-3-phenyl-2-pyrrolidone (*q.v.*). The amide crystallised from water in needles, m. p. 125° (Found: C, 71·4; H, 8·3; N, 12·2. $C_{13}H_{18}ON_2$ requires C, 71·6; H, 8·3; N, 12·8%). The hydrochloride had m. p. 247° (Found: C, 60·9; H, 7·4; N, 10·9; Cl, 14·0. Calc. for $C_{13}H_{19}ON_2,HCl$: C, 61·3; H, 7·5; N, 11·0; Cl, 14·0%).

Ethyl 4-Phenyl-1-ethylpiperidine-4-carboxylate (V; R = R′ = Et).—The dibromo-ethyl ester (IV; R = Et) (12 g.) and 28% w/v ethyl-alcoholic ethylamine (45 ml.) were heated under pressure for 3 hours at 90—95°. The ethereal extract, obtained as described above for the methyl ester, gave a first fraction, b. p. 182—195°/15 mm., which yielded a *hydrochloride*, very soluble in water but crystallising from alcohol–ether in octagonal plates, m. p. 171° (Found: C, 64·5; H, 7·8; N, 5·1; Cl, 12·4. $C_{16}H_{23}O_2N,HCl$ requires C, 64·6; H, 8·1; N, 4·7; Cl, 11·9%).

Ethyl 4-Phenyl-1-n-propylpiperidine-4-carboxylate (V; R = Et, R′ = *n*-C_3H_7).—The ethyl ester (IV; R = Et) (5 g.) and *n*-propylamine (8 ml.), warmed under reflux for 2 hours and worked up as previously described, gave a fraction (2 g.), b. p. 190—203°/20 mm., which formed a *hydrochloride* crystallising from alcohol–ether in hexagonal prisms, m. p. 196° (Found: C, 65·5; H, 8·2; N, 4·8; Cl, 11·4. $C_{17}H_{25}O_2N,HCl$ requires C, 65·5; H, 8·4; N, 4·5; Cl, 11·4%).

Ethyl 4-Phenyl-1-n-butylpiperidine-4-carboxylate (V; R = Et, R′ = *n*-C_4H_9).—The same ester (10 g.) and *n*-butylamine (10 g.), refluxed for 3 hours and worked up as described above, gave a fraction (1·8 g.), b. p. 225—230°/13 mm., which was only partly soluble in acid. The base was therefore extracted with hydrochloric acid and, after being washed with ether, the aqueous solution was evaporated. The resulting *hydrochloride* crystallised from alcohol–ether in prisms, m. p. 183° (Found: N, 4·4; Cl, 10·9. $C_{18}H_{27}O_2N,HCl$ requires N, 4·3; Cl, 10·9%).

Ethyl 4-Phenyl-1-benzylpiperidine-4-carboxylate (V; R = Et, R′ = C_7H_7).—The ester (IV) (10 g.) and benzylamine (20 g.) gave the hydrochloride, m. p. 242°, as square leaflets from water (Found: Cl, 9·9. Calc. for $C_{21}H_{25}ON_2,HCl$: Cl, 9·9%) (cf. Eisleb, *loc. cit.*).

α-(β′-Aminoethyl)-α-phenylbutyrolactone (VIII; R = R′ = H) *and 3-(β-Hydroxyethyl)-3-phenyl-2-pyrrolidone* (VI; R = H).—The bromo-lactone (VII; X = Br) (10 g.) and saturated ethyl-alcoholic ammonia (40 ml.) were heated under pressure for 3 hours at 90—95°. After removal of alcohol, the residue was treated with water (90 ml.) and dilute hydrochloric acid until just blue to Congo-paper, and left overnight. The resulting solid, consisting of 3-*(β-hydroxyethyl)-3-phenyl-2-pyrrolidone*, crystallised from water in needles (4·3 g.), m. p. 85—90°, containing water of crystallisation, and from benzene in hexagonal leaflets, m. p. 111—112° (Found: C, 70·2; H, 7·3; N, 7·1. $C_{12}H_{15}O_2N$ requires C, 70·2; H, 7·3; N, 6·8%). The pyrrolidone was insoluble in dilute hydrochloric acid, but with concentrated acid it formed *α-(β′-aminoethyl)-α-phenylbutyrolactone hydrochloride*, which crystallised from alcohol–ether in needles, m. p. indefinite (75—150°) (Found: C, 55·7; H, 6·9; N, 5·4; Cl, 13·8. $C_{12}H_{15}O_2N,HCl,H_2O$ requires C, 55·5; H, 6·9; N, 5·4; Cl, 13·7%). The hydrochloride was very soluble in water, forming a stable neutral solution, but with alkali it reverted to the pyrrolidone.

* Attempts to isolate the free acid were unsuccessful, as the oil, on acidification, although at first soluble in alkali, rapidly became insoluble during extraction, etc.

α-(β'-Methylaminoethyl)-α-phenylbutyrolactone (VIII; R = H, R' = Me).—The bromo-lactone (5 g.) and 27% methyl-alcoholic methylamine (20 ml.) were heated under pressure at 90—95° for 3 hours. The alcohol-free residue was made strongly alkaline and extracted with ether. In this way, the methylamino-lactone was obtained as an oil, b. p. 225—240°/17 mm. (slight decomp.). The methylamino-lactone was also obtained as a second fraction in the preparation of (V; R = Me or Et, R' = Me) (*q.v.*). Its *hydrochloride* crystallised from alcohol–ether in hexagonal prisms, m. p. 178° (Found: C, 61·1; H, 6·9; N, 5·5; Cl, 14·2. $C_{13}H_{17}O_2N$,HCl requires C, 61·1; H, 7·0; N, 5·5; Cl, 13·9%). Heated with *p*-nitrobenzoyl chloride at 150—200° for 1 minute, the hydrochloride gave a p-*nitrobenzamido*-derivative, which crystallised from alcohol in prisms, m. p. 151° (Found: C, 65·0; H, 5·5; N, 7·8. $C_{20}H_{20}O_5N_2$ requires C, 65·2; H, 5·4; N, 7·6%). On the other hand, when heated alone up to 280°, it evolved hydrogen chloride, leaving a residual oil, which failed to solidify. The oil, probably 3-phenyl-1-methyl-3-(β-hydroxyethyl)-2-pyrrolidone (VI; R = Me), dissolved in concentrated hydrochloric acid, but reappeared on dilution. It formed a p-*nitrobenzoate* crystallising from alcohol in rectangular plates, m. p. 110—112° (Found: C, 65·2; H, 5·6; N, 7·8. $C_{20}H_{20}O_5N_2$ requires C, 65·2; H, 5·4; N, 7·6%).

α-(β'-Ethylaminoethyl)-α-phenylbutyrolactone (VIII; R = H, R' = Et).—The bromolactone (5 g.) and 28% ethyl-alcoholic ethylamine (20 ml.), worked up as described in the previous example, yielded the ethylamino-lactone as an oily base, which was also obtained as a residual oil in the preparation of (V; R = R' = Et) (*q.v.*). On heating under reflux at normal pressure for 10—15 minutes, it showed signs of changing into the corresponding lactam of type (VI). The crude base formed a *hydrochloride*, which crystallised from alcohol–ether in rectangular plates (1·9 g.), m. p. 194° (Found: C, 62·3; H, 7·1; N, 5·3; Cl, 13·5. $C_{14}H_{19}O_2N$,HCl requires C, 62·3; H, 7·4; N, 5·2; Cl, 13·2%).

α-(β'-n-Propylaminoethyl)-α-phenylbutyrolactone (VIII; R = H, R' = *n*-C_3H_7) *and 3-Phenyl-3-(β-hydroxyethyl)-1-n-propyl-2-pyrrolidone* (VI; R = *n*-C_3H_7).—A mixture of the bromo-lactone (5 g.) and *n*-propylamine (10 g.) was left for 12 hours and then refluxed for 2 hours. After removal of the excess of *n*-propylamine, the mixture was made alkaline to indigo-carmine and extracted with ether. The ether-free extract was dissolved in concentrated hydrochloric acid, the solution evaporated to dryness to remove excess of acid, and again treated with water; it then only partly redissolved. The resulting water–oil mixture was extracted with ether to give an aqueous portion (A), and an ethereal extract (B). The portion (A), on repeated evaporation with alcohol, eventually yielded the *hydrochloride* of *α-(β'-n-propylaminoethyl)-α-phenylbutyrolactone* as a solid, which crystallised from alcohol–ether in needles (0·2 g.), m. p. 167—168° (Found: C, 63·5; H, 7·7; N, 5·1; Cl, 12·5. $C_{15}H_{21}O_2N$,HCl requires C, 63·5; H, 7·8; N, 4·9; Cl, 12·5%). The extract (B) was dried and distilled in a vacuum. The first fraction up to 220° contained diminishing traces of halogen and became increasingly soluble in concentrated hydrochloric acid. The second fraction, b. p. 228—230°/11 mm., was a colourless halogen-free syrup, consisting of *3-phenyl-3-(β-hydroxyethyl)-1-n-propyl-2-pyrrolidone* (Found: C, 72·3; H, 8·4; N, 6·1. $C_{15}H_{21}O_2N$ requires C, 72·9; H, 8·5; N, 6·1%). It dissolved readily in cold concentrated hydrochloric acid, but reappeared as an oil on dilution.

α-(β'-Diethylaminoethyl)-α-phenylbutyrolactone (VIII; R = R' = Et).—The bromo-lactone (7 g.), diethylamine (10 ml.), and alcohol (10 ml.), heated under pressure at 90—95° for 4 hours and worked up in the usual manner, yielded *α-(β'-diethylaminoethyl)-α-phenylbutyrolactone* as an oily base, b. p. 214—220°/17 mm. (Found: C, 73·5; H, 8·8; N, 5·4. $C_{16}H_{23}O_2N$ requires C, 73·6; H, 8·8; N, 5·4%). The *hydrochloride* was obtained as an uncrystallisable syrup (Found: Cl, 11·9. $C_{16}H_{23}O_2N$,HCl requires Cl, 11·9%). Attempts to prepare it in crystalline form by passing dry hydrogen chloride into an ethereal solution of the base were unsuccessful.

α-(β'-Piperidinoethyl)-α-phenylbutyrolactone (VIII; RR' = C_5H_{10}).—A mixture of the bromo-lactone (3 g.) and piperidine (3 g.), refluxed for 3 minutes and then worked up in the usual way, gave the hydrochloride, which crystallised from alcohol–ether in rhombs, m. p. 216—218° (Found: C, 66·1; H, 7·4; N, 5·0; Cl, 11·5. Calc. for $C_{17}H_{23}O_2N$,HCl: C, 65·9; H, 7·7; N, 4·5; Cl, 11·5%).

α-(β'-Methylanilinoethyl)-α-phenylbutyrolactone (VIII; R = Me, R' = Ph).—The bromo-lactone (5 g.) and methyl-aniline (10 ml.) were refluxed for 3 hours and then steam-distilled to remove excess of methylaniline. The residue was basified, and the ethereal extract again steam-distilled to remove the remaining traces of methylaniline. The residual oil was now strongly acidified with hydrochloric acid—most of the oil dissolved—cleaned with ether, and the aqueous layer evaporated to dryness. The residual gum solidified on treatment with alcohol–ether to *α-(β'-methylanilinoethyl)-α-phenylbutyrolactone hydrochloride*, which crystallised from the same solvents in hexagonal prisms (2·4 g.), m. p. 160—165° (Found: N, 4·5; Cl, 10·4. $C_{19}H_{21}O_2N$,HCl requires N, 4·2; Cl, 10·7%). The hydrochloride was soluble in water in high concentration, giving an acid solution, but on dilution the base was liberated as an oil.

α-(β'-Benzylmethylaminoethyl)-α-phenylbutyrolactone (VIII; R = Me, R' = CH_2Ph).—The bromo-lactone (2 g.) and benzylmethylamine (3 ml.) were heated together for 2—3 minutes, the internal temperature being allowed to rise to 195°. After cooling, the mixture was made alkaline to indigo-carmine, and the ethereal extract treated with sodium sulphate and bicarbonate to remove caustic alkali. The residue was then repeatedly evaporated with water in a vacuum in an attempt to remove traces of benzylmethylamine. After several experiments, the following method of working up was found to give the best results: The oil was redissolved in ether and fractionally extracted with small quantities of dilute hydrochloric acid. The first acid extraction (alkaline reaction) gave hydrochloride, m. p. 115—155°. The second acid extraction (still alkaline) gave crude benzylmethylamine hydrochloride, m. p. 170—176°. The third extraction (approaching neutrality) yielded a similar product. The fourth extraction, however, a very slight excess of dilute hydrochloric acid being used, gave crude *α-(β'-benzylmethylaminoethyl)-α-phenylbutyrolactone hydrochloride* (1·6 g.), which crystallised from alcohol–ether in minute rectangular prisms, m. p. 165—166° (Found: C, 69·2; H, 7·0; N, 4·3; Cl, 10·5. $C_{20}H_{23}O_2N$,HCl requires C, 69·5; H, 7·0; N, 4·1; Cl, 10·3%). The hydrochloride was very soluble in water, giving neutral solutions. Careful addition of a little concentrated hydrochloric acid threw out the hydrochloride as an oil, but it redissolved on further addition of this acid.

3-Phenyl-3-(β-hydroxyethyl)-1-n-butyl-2-pyrrolidone (VI; R = *n*-C_4H_9).—The bromo-lactone (10 g.) and *n*-butylamine (10 g.) were heated together on the steam-bath for 3 hours. The product was made strongly alkaline and extracted with ether. The extract was dried and evaporated, and the residue dissolved in concentrated hydrochloric acid. The resulting solution, on dilution with water, gave an oil, which on extraction and distillation yielded the *pyrrolidone* (2·5 g.) as a fraction, b. p. 234—236°/12 mm. (Found: C, 73·7; H, 8·8; N, 5·4. $C_{16}H_{23}O_2N$ requires C, 73·6; H, 8·8; N, 5·4%). In properties it resembled its propyl analogue (*q.v.*).

1 : *3-Diphenyl-3-(β-hydroxyethyl)-2-pyrrolidone* (VI; R = Ph).—The bromo-lactone (3 g.) was boiled with an excess of aniline for 3 minutes. Dilute hydrochloric acid was added to remove aniline, and the remaining oil cooled and scratched until it solidified. Crystallised from benzene–petrol, it gave the *pyrrolidone* in octagonal tablets (2·3 g.), m. p. 100—101° (Found: C, 77·0; H, 6·8; N, 5·4. $C_{18}H_{19}O_2N$ requires C, 76·9; H, 6·8; N, 5·0%). The pyrrolidone dissolved in warm concentrated hydrochloric acid, but separated unchanged on cooling. There was no reaction with methyl iodide. Its p-*nitrobenzoate* crystallised from alcohol in hexagonal prisms, m. p. 136—137° (Found: C, 69·7; H, 5·0; N, 6·5. $C_{25}H_{22}O_5N_2$ requires C, 69·7; H, 5·1; N, 6·5%).

3-Phenyl-1-cyclohexyl-3-(β-hydroxyethyl)-2-pyrrolidone (VI; R = C_6H_{11}), obtained by similar methods from the bromo-lactone and *cyclo*hexylamine, crystallised from benzene–petrol in minute tablets, m. p. 61°, which dissolved in

cold concentrated hydrochloric acid, but came out on dilution (Found: C, 75·5; H, 9·0; N, 5·1. $C_{18}H_{25}O_2N$ requires C, 75·3; H, 8·8; N, 4·9%).

3-Phenyl-1-benzyl-3-(β-hydroxyethyl)-2-pyrrolidone (VI; R = C_7H_7), obtained from the bromo-lactone and benzylamine (spontaneous reaction above 90°), crystallised from benzene–petrol in small needles, m. p. 123—124° (Found: C, 77·3; H, 7·2; N, 5·0. $C_{19}H_{21}O_2N$ requires C, 77·3; H, 7·1; N, 4·7%).

Sincere thanks are due to Mr. A. Bennett for microanalyses, and to Mr. R. R. G. Hicks for assistance in the experimental work.

DEVELOPMENT LABORATORIES, WELLCOME CHEMICAL WORKS, DARTFORD. [*Received, February 19th*, 1945.]

NOTES.

Apparatus for Microtitrations with a Glass Electrode. By J. R. CATCH, A. H. COOK, and J. A. KITCHENER.

DETAILS are given of a simple apparatus which has been used for some years with satisfactory results for the microtitration of biological products, sulphonamides, determination of p*K* values, detection of latent acid groupings, etc. The titration cell consists of a tube *A* (Fig. 1) sealed at one end to a capillary *B*. The internal diameter of *A* is slightly larger than the external diameter of a sealed glass electrode *C* (Cambridge Instrument Co.); *B* is filled throughout its length with 2% agar gel in saturated aqueous potassium chloride and is of very narrow bore so that diffusion of solution

FIG. 1.

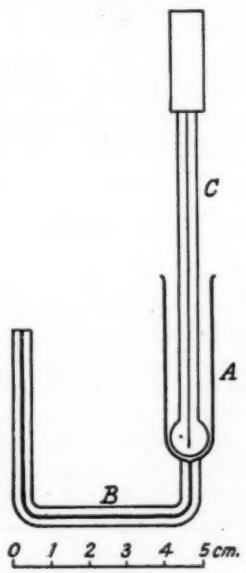
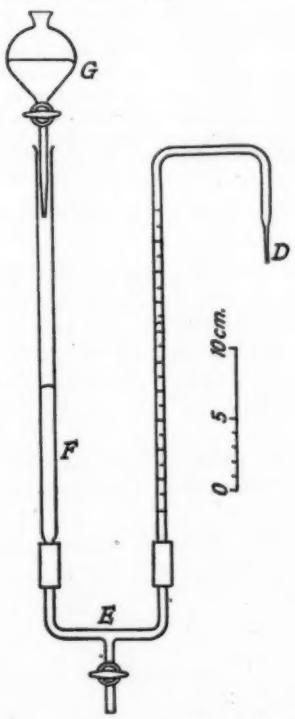


FIG. 2.



from *A* into *B* is negligible; *A* is thus virtually closed at its lower end and carries a conducting bridge. The titration can be carried out in an inert atmosphere if desired by passing nitrogen from a capillary through *A*. The sample (2—5 mg.) under examination is weighed into *A* and dissolved in 0·1—0·2 c.c. of water or other solvent which is sufficient to surround the bulb of the electrode. Sparingly soluble acids or bases may be titrated as a finely divided suspension: this does not affect the observed value of the equivalent, though the shape of the titration curve may be modified as the sample passes into solution. The open end of *B* is connected in the ordinary way through a potassium chloride salt bridge to a calomel electrode, and the e.m.f. of the whole cell is measured on a valve electrometer–pH meter.

Additions of acid or alkali are made from micro-burettes of the type shown in Fig. 2, and it is convenient to set them up in pairs so that back-titrations can be carried out without disturbing any part of the apparatus. The burettes consist of 1-c.c. graduated pipettes sealed to a tube with a fine but stout capillary tip *D*. When filled, the burettes are adjusted so that this tip projects into the cell *A* and touches the wall a little above the resting level of the bulb of *C*. Diffusion of acid or alkali from *D* into the liquid contents of *A* is undetectable if *D* is a very narrow capillary. The lower end of each burette is connected, by tubing carrying a tap *E*, with a wide tube *F* into which mercury is run from a dropping-funnel *G*. The apparatus is filled by first filling it with mercury and then opening *E* whilst *D* is held below the level of the acid or alkali. Expulsion from *D* is controlled by additions of mercury from *G* through its capillary outlet and there is no difficulty in delivering quantities of reagent of about 0·01 c.c. which can be read to the nearest 0·001 c.c. Rubber pressure-tubing connections at *E* give flexibility but in no way disturb the stability and reproducibility of the volume readings. After each addition of alkali or acid, mixing in *A* is effected by a few passages of *C* up and down the closely fitting walls of *A*, after which the pH readings are taken, and a titration curve constructed in the normal

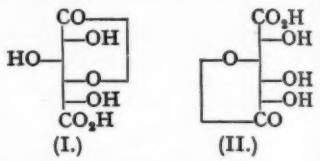
way. In using N/20-acid or -alkali to titrate or back-titrate known simple compounds such as benzoic acid, the accuracy in determining the equivalent value is about 1 in 500 and therefore compares favourably with the macrotitrimetric procedure. Of especial value, however, is the possibility of constructing complete titration curves by using only micro-quantities of material and inexpensive adjuncts.

The authors thank Professor I. M. Heilbron, D.S.O., F.R.S., for his interest and encouragement.—IMPERIAL COLLEGE OF SCIENCE AND TECHNOLOGY, LONDON, S.W.7. [*Received, January 20th,* 1945.]

The Constitution of the Two Lactones of d-*Glucosaccharic Acid.* By T. REICHSTEIN.

SMITH recently expressed the opinion (J., 1944, 571) that the lactone, m. p. 133°, of Sohst and Tollens (*Annalen*, 1888, **245**, 1) is a mixture of *d*-glucosaccharo-1 : 4-lactone (I) and *d*-glucosaccharo-3 : 6-lactone (II). This opinion is based on the fact that by prolonged treatment of the above-mentioned lactone with methyl iodide and silver oxide he was able to isolate the tetramethyl derivatives of (I) and (II) in moderate yields. Considerable quantities of other products were formed in the reaction, three of which were isolated in a state of purity, thus proving that the methylation process was accompanied by rearrangements and degradations.

The lactone, m. p. 133°, was long considered to possess formula (I) (Fischer and Piloty, *Ber.*, 1891, **24**, 521) until Schmidt, Zeiser, and Dippold (*Ber.*, 1937, **70**, 2402) produced strong evidence in support of formula (II), the correctness of which was proved by Schmidt and Günthert (*Ber.*, 1938, **71**, 493) by smooth cleavage with periodic acid and confirmed by Sutter and Reichstein (*Helv. Chim. Acta*, 1938, **21**, 210) by the results of reduction with sodium amalgam. The last-named authors also showed that the second *d*-glucosaccharolactone, isolated as a hydrate, m. p. *ca.* 90°, by Reichstein, Grüssner, and Oppenauer (*Helv. Chim. Acta*, 1933, **16**, 1032) very probably possesses formula (I) (only the size of the lactone ring was not definitely proved) and that (I) and (II) can be separated by fractional crystallisation, although with some difficulty; it was found that from supersaturated solutions of the pure compounds and of mixtures only that compound crystallised which had been used for inoculation, and that (I) and (II) differ greatly in solubility.



(I.) (II.)

In the light of these facts, the present writer finds it difficult to assume that the lactone of higher m. p. (135—136° according to Schmidt, Zeiser, and Dippold, *loc. cit.*, and to Sutter and Reichstein, *loc. cit.*) is a mixture and inclines to the view that a partial isomerisation of (II) may have occurred during the methylation process.—PHARMAZEUTISCHE ANSTALT DER UNIVERSITÄT, BASEL. [*Received, March* 1*st,* 1945.]

ONE HUNDRED AND FOURTH ANNUAL GENERAL MEETING.

THE One Hundred and Fourth Annual General Meeting of the Chemical Society was held at Burlington House on Thursday, April 19th, 1945, at 11.30 a.m., the President, Professor W. N. Haworth, D.Sc., F.R.S., in the Chair.

The notice convening the meeting was read.

The President read a letter received from Academician N. Derzhavin, conveying greetings from fellow scientists in Latvia and drawing attention to the crimes committed by the German invaders on the Latvian people. His proposed reply was read and endorsed. With the approval of Fellows present, the President agreed to convey the deep sympathy of the Council to the American Chemical Society on the loss of their great national leader, whose death is lamented throughout the world, and also greetings to the Belgian, French, and Russian Chemical Societies, expressing our joy at the liberation of their Countries from the foreign invader.

In presenting the Report of Council for 1944, copies of which were available, Professor G. M. Bennett dealt briefly with the activities of the Society during 1944, mentioning in particular that papers had been held up from publication owing to lack of paper, but that the position was now improving. He paid tribute to the staff and in conclusion referred to the retirement of the General Secretary and to the following resolution passed by the Council :—

> " The Council has received with profound regret the news of the coming retirement of Mr. S. E. Carr from the office of General Secretary. It desires to place on record its deep feeling of gratitude for the great services he has rendered to the Society over a period of 42 years."

He dwelt on the happy relations that had always existed between the Officers, Council and Fellows and Mr. Carr.

In dealing with the Accounts for 1944, the Treasurer explained that owing to war conditions it had been found impossible to present audited accounts in time for the meeting. It would be necessary, therefore, to adjourn the meeting until Thursday, 17th May, at 5 p.m., when audited accounts would be ready. After dealing with the Accounts in some detail, the Treasurer paid his tribute to the work of Mr. Carr and his staff and also to Mr. Morris and the staff at the Conjoint Chemical Office.

The adoption of the Report of Council for 1944 was proposed by Dr. R. W. West, seconded by Dr. W. R. Angus, and carried.

It was declared that Professor H. V. A. Briscoe had been elected as Honorary Secretary, and Dr. Brynmor Jones and Professor J. M. Robertson as Elected Ordinary Members of Council for Constituencies IV and V respectively.

The report of the Scrutators on the ballot for Vice-Presidents who have not filled the office of President, and for Elected Ordinary Members of Council for Constituencies I, II, and III was presented, and it was declared that the following had been elected :—

Vice-Presidents, who have not filled the office of President :

Professor A. J. Allmand, Professor J. W. Cook, and Professor I. M. Heilbron.

Elected Ordinary Members of Council :

Constituency I (South-East England) :

Mr. R. P. Bell, Dr. R. J. W. Le Fèvre, and Professor A. R. Todd.

Constituency II (Central and South-West England and South Wales) :

Professor Wilson Baker, Professor H. T. S. Britton, and Dr. Maurice Stacey.

Constituency III (North-West England, North Wales, and the Isle of Man) :

Dr. Donald H. Hey and Dr. Frank S. Spring.

A vote of thanks to the Vice-Presidents, Treasurer, Honorary Secretaries, Council and Committees for their services during the past year, proposed by Professor S. Sugden and seconded by Dr. Brynmor Jones was carried, acknowledgment being made by Professor A. Findlay.

On the motion of Professor J. E. Coates, seconded by Dr. J. Bell, Messrs. W. B. Keen & Co., were elected Auditors to audit the accounts for 1945.

The President stated that Professor T. S. Moore had written expressing his apologies for absence from the meeting. Reference was made to Professor Moore's retirement from the office of Chairman of the Publication Committee and on a motion from the Chair a hearty vote of thanks to Professor Moore for the valuable services he had rendered to the Society during his term of office was carried with acclamation. The President stated that Professor C. N. Hinshelwood had accepted the Council's invitation to this important office.

The meeting was then adjourned.

A luncheon, attended by Fellows, was held at Stewart's Restaurant at 1 p.m.

The meeting was resumed at 2.30 p.m.

In presenting the Longstaff Medal for 1945 to Professor N. V. Sidgwick, the President stated that the award was made primarily as a recognition of his outstanding work as an exponent of the electronic theory of valency, and of the leadership he had given in the generalisation of relations between electronic structure and chemical properties over the whole domain of chemistry. In acknowledging the award, Professor Sidgwick expressed his pride at receiving the award and at the inclusion of his name among the distinguished holders of the Longstaff Medal.

The Harrison Memorial Prize for 1944 was presented to Dr. Leslie F. Wiggins, and in making the presentation the President said that the Prize was awarded to a Chemist of either sex who shall not be more than thirty years of age and who, during the previous five years, shall have conducted the most meritorious and promising original investigation in Chemistry and published the results of such work. Dr. Wiggins made suitable acknowledgment.

The President then delivered his Presidential Address entitled "Starch." At its conclusion, a vote of thanks to him for his services in the Chair and for his Address, with the request that he would allow his Address to be printed in the *Journal*, was proposed by Professor F. G. Donnan, seconded by Dr. J. L. Simonsen, and carried with acclamation.

The meeting was adjourned.

REPORT OF COUNCIL FOR 1944.

The Council sent suitable replies to greetings and messages of goodwill received from the U.S.S.R. Society for Cultural Relations with Foreign Countries and from the Meeting of Soviet Scientists held in Moscow on 18th June. The Council also sent their good wishes to the All Union Chemical Society on the occasion of the meetings held in Moscow to celebrate Mendeléev's discovery of the Periodic Classification of the Elements.

Honorary Secretaryship. The Council received with regret in June the resignation of Professor C. W. Davies from the office of Honorary Secretary. They recorded their high appreciation of the services he had rendered to the Society during eight difficult years he had held office. In November, Professor H. V. A. Briscoe was appointed to this office until the next Annual General Meeting.

Retirement of General Secretary. The Council have received with regret an intimation from Mr. S. E. Carr of his wish to retire from the office of General Secretary during the summer and have passed the following resolution :—

> "The Council has received with profound regret the news of the coming retirement of Mr. S. E. Carr from the office of General Secretary. It desires to place on record its deep feeling of gratitude for the great services he has rendered to the Society over a period of 42 years."

I. FELLOWSHIP.

1. *Fellowship Statistics.* The number of Fellows on the 31st December, 1943, was 5232. During 1944, 730 Fellows were elected and 47 reinstated, the corresponding figures in 1943 being 543 and 31, respectively. The Society has lost 2 Fellows killed by enemy action, 48 by death, 35 by resignation, and 39 by removal for non-payment of annual subscriptions—a total loss of 124, compared with 168 in 1943. The number of Fellows on the 31st December, 1944, was 5885. Of these 2382 are joint members of the three Chartered Bodies and 736 are members of the two publishing Societies. Of those who became joint members of the three bodies in 1944, 358 are new Fellows of the Chemical Society and of those who became joint two-body members, 147 are new Fellows. The number of joint members of the three bodies has increased during the year by 497, of the joint members of two bodies by 171, and the number of single-body Fellows has decreased by 15.

2. *Joint Student Facilities.* During 1944, 28 persons have been granted joint student facilities by the two publishing Societies under the Chemical Council Scheme.

3. *Deaths.* The Council mourn the death of Sir Prafulla C. Rây, who was elected an Honorary Fellow in November, 1933. Among prominent Fellows whose deaths the Council have also to record are Sir John J. Fox, Dr. I. S. Maclean, and Dr. F. L. Pyman, who had taken an active part in the Society's affairs by serving on the Council and on Committees. Mr. R. O. Jones and Dr. J. N. Sugden lost their lives in air raids.

II. PUBLICATIONS.

1. *Journal.* During the year 242 papers were received by the Society; of these 3 were declined.

The *Journal* for 1944, occupying 679 pages, contains 184 papers (21 on General, Physical and Inorganic Chemistry, and 163 on Organic Chemistry), 15 notes, and 5 lectures, in addition to Obituary Notices (30 pages) and the Report of the Annual General Meeting (25 pages). The corresponding figures for 1943 are 662 pages, 175 memoirs, 14 notes, and 3 lectures. Owing to war conditions the monthly parts of the *Journal* were issued several weeks late during 1944; it is hoped that during 1945 it will be possible to get the date of issue back to the usual time, namely, the last day of the month.

The question of publishing Obituary Notices of Fellows in a separate volume is under consideration.

2. *Tables of Isotopic Weights.* It has been decided that tables of Isotopic Weights of stable isotopes, with figures for the relative abundance of each, shall be published at regular intervals in the *Journal.*

3. *Annual Reports.* Volume XL (1943) of the *Annual Reports on the Progress of Chemistry,* which again owing to war conditions was not issued until August, contains 253 pages as against 255 pages in Volume XXXIX for 1942. The amount of paper available was not sufficient to meet the demand even though the length was much reduced.

4. *Reservation of Publications.* In reply to requests received from institutions abroad for the reservation of publications of the Society issued during the War, it has been decided that no reservation can be made until the requirements of Fellows who have been On Service has been met after the end of the War, and until it is possible to consider all such claims together.

5. *Co-ordination of Publications.* A questionnaire dealing with the Co-ordination of Chemical Publications received from the Chemical Council is under consideration.

III. MEETINGS.

1. *Scientific Meetings.* During 1944 six meetings were held in London and thirty-four outside London. A list of these is given in Appendix B.

2. *Annual General Meeting.* The Hundred and Third Annual General Meeting was held in London on the 20th April and a report appeared in the *Journal* for April.

IV. LIBRARY.

1. The Annual Report of the Joint Library Committee for 1944 appears as Appendix A.

2. *Reference Books.* The question of decreasing the number of "Reference Books" (*i.e.*, books that cannot be borrowed) in the Library was considered. The number of books in the library thus classified had recently been considerably reduced and it was not thought advisable to effect any further reduction.

3. *Appointment of Librarian.* In May, Mr. A. E. Cummins was appointed Librarian in succession to the late Mr. F. W. Clifford.

V. ADMINISTRATION.

1. *Local Representatives.* The resignations of Dr. J. W. Baker, Dr. S. Peat, Dr. G. R. Ramage, and Dr. R. Fraser Thomson from the office of Local Representative for Leeds, Birmingham, North Wales, and Manchester, respectively, have been accepted with regret; Dr. F. R. Goss, Dr. L. L. Bircumshaw, Dr. W. R. Angus, and Dr. J. C. Withers were appointed to fill the vacancies.

2. *Accommodation.* The question of seeking further accommodation has been actively pursued by the Council. In May, the Society was represented at a Conference of the Learned Societies in Burlington House called by the Royal Society to consider approaching the Government on the matter, and in October the Government received a deputation consisting of the President of the Royal Society, together with representatives of all the Societies in Burlington House and of six other Societies. The imperative need for the housing of all the Learned Scientific Societies on a central site in London under one roof was emphasised, and the Government was asked to meet this urgent situation by providing such site with adequate buildings both for the present and for future expansion.

The deputation was received with sympathy by the Government, who requested that they should be furnished with full details of a co-ordinated scheme that would meet the requirements of all the Learned Societies concerned.

VI. FINANCE.

1. *Insurance.* Fire and War Damage Insurances on the Library and on publications have been increased by £350 and £550, respectively, and insurance on Standing Type and on Manuscript by £190 and £40, respectively.

2. *Investments.* The following investments have been made during the year :—

£3,000 on Special Reserve for Publications in 2½% National War Bonds, 1952—1954.
£700 on Special Reserve for the Research Fund in 2½% National War Bonds, 1952—1954.
£300 on Staff Pensions in 3% Savings Bonds, 1960—1970.

The Society's holdings of £11,672 16*s.* 4*d.* in 5% Conversion Loan was re-invested in Local Loans 3% Stock; £300 of the £500 standing on Special Reserve for the Library was deposited with the London Savings Bank, and of the £1,000 standing to the credit of the Special Publications Fund, £500 was deposited with the Post Office Savings Bank and £500 with the London Savings Bank. These deposits were made so that the money would be easily available when required.

3. *Contributions.* The Council received £1,050 from the Chemical Council; also, through the Royal Society £500 from the Rockefeller Foundation and £200 from the Government Grant towards the cost of publications. They were notified that Messrs. Genatosan have entered into a deed of covenant to contribute £25 a year for seven years to the Library. The Council record their thanks for these substantial contributions and to those Fellows who generously continue to support the Publications Fund.

4. *Bequests.* Under the Will of the late Mr. Percy Appleyard, who died on the 10th October, 1943, the Society will receive one-third of the residue of his estate, subject to certain life interests and to the payment of certain pecuniary legacies, the income of such residue to be applied as to one-half to the Publications Fund and one-half to the Research Fund.

As stated in the Report of Council for 1940, under the Will of the late Sir Gilbert T. Morgan the income from his residuary estate was left to the Society, subject to life interests, and on certain conditions. The death of Lady Morgan took place on the 11th March, and the Council have accepted the bequest and have agreed to administer the funds in accordance with the conditions set out in the Will. The question has been raised by the Public Trustee as to whether the words in the Will " to assist in the unification of the Chemical profession within the British Empire" can be considered as a bequest for charitable purposes, and this question is at present before the High Court.

The following form of bequest has been approved by the Council :—

"I..... of .....give and bequeath to The Chemical Society, Burlington House, Piccadilly, London, W.1, free from deduction on account of any and every kind of death duty the sum of.....for the use of The Chemical Society in such manner as the Council may in its absolute discretion determine. The receipt of the Treasurer or other Officer for the time being of The Chemical Society shall be a sufficient discharge for the same."

INCOME AND EXPENDITURE GENERAL PURPOSES ACCOUNT FOR THE YEAR ENDED 31ST DECEMBER, 1944.

Income.

1943 £ s. d.	£ s. d.		1944 £ s. d.	£ s. d.
	45 0 0	To Life Composition Fees (£223 10*s.* 0*d.*), one-third as Income		74 10 0
		„ Annual Subscriptions :		
		Single-body Fellows—		
1,165 12 3		Received in advance, on account of 1944	866 6 4	
4,475 14 6		Received during 1944 on account of 1944	4,433 10 0	
364 11 6		Received during 1944 on account of 1943	332 11 4	
76 1 6		Received during 1944 on account of 1942 and previous years	31 15 7	
		Joint Fellows—		
460 10 3		Received in advance on account of 1944	802 7 1	
4,622 9 4		Received on account of 1944	5,362 14 9	
67 4 10		Received during 1944 on account of 1943 and previous years	89 15 8	
11,232 4 2			11,919 0 9	
		Less Payment to the Society of Chemical Industry to adjust cost of publications supplied to Joint Members	186 0 0	
163 10 0			11,733 0 9	
11,068 14 2				
		Less Amount included in last year's Income, being valuation of Arrears as per last Balance Sheet	350 0 0	
350 0 0			11,383 0 9	
10,718 14 2				
		Add Arrears to date (£707 19*s.* 0*d.*) Estimated to realise as per Balance Sheet	350 0 0	
350 0 0		Subscriptions in suspense (£2437 14*s.* 2*d.*)		
	11,068 14 2			11,733 0 9
	493 4 7	„ Dividends on Investments		488 17 3
	466 14 2	„ Income Tax recovered		465 4 9
	60 0 0	„ Donations		
	52 13 8	„ Miscellaneous Receipts		60 6 2
	£12,186 6 7			£12,821 18 11

Expenditure.

1943 £ s. d.	£ s. d.		1944 £ s. d.	£ s. d.
		By Administration Expenses :		
3364 2 1		Office Salaries and Wages	3796 6 10	
172 5 11		Superannuation	177 3 0	
312 4 8		House Expenses, etc.	317 9 1	
84 0 0		Accountants' Charges	84 0 0	
390 0 0		Printing, Stationery and Office Expenses ...	410 14 4	
142 6 5		Postages	160 10 8	
61 11 4		Miscellaneous	92 16 1	
4526 10 5			5039 0 0	
		Less Transfer to Publications and Library :	£ s. d.	
356 12 0		Journal	522 17 2	
147 13 0		Abstracts A I	213 19 2	
147 13 0		„ A II	213 19 2	
147 13 0		„ A III	213 19 1	
		Annual Reports	87 10 5	
238 2 3		Library Account	302 8 7	
	3488 17 2		1554 13 7	3484 6 5
	167 15 5	„ Expenses on Account of Conjoint Chemical Office		202 19 7
	40 19 4	„ Expenses of Meetings		73 13 0
	5 5 0	„ Donation		30 5 0
	6452 13 9	„ Balance of Expenditure on Publications to Publications Fund		6261 12 9
		„ Contribution to Library Fund :		
850 9 4		For Fittings, Furniture, Books, Periodicals, and Binding	978 2 4	
39 0 6		For Air Raid Precautions	27 5 6	
197 15 4		For War Damage Insurance	119 10 9	
346 8 4		Proportion of Maintenance	291 2 10	
1433 13 6			1416 1 5	
230 6 0		*Less* Balance from Library Account		
	1203 7 6			1416 1 5
	300 0 0	„ Transfer to Staff Pensions Fund		900 0 0
	124 15 5	„ Expenses of Local Representatives		103 11 7
		„ Legal Expenses		26 5 0
	136 19 11	„ Air Raid Precautions		113 0 4
	120 18 6	„ Travelling Expenses of Members of Council ...		102 12 9
		„ Loss on Exchange (Australia)		33 14 6
		„ War Damage Insurance	202 12 1	
332 4 5		*Less* Transfer to Publications and Library :	£ s. d.	
44 18 11		Journal	28 3 4	
20 11 11		Abstracts A I	12 17 11	
20 11 11		„ A II	12 17 11	
3 15 2		„ A III	2 7 6	
197 15 4		Library Account	119 10 9	
	44 11 2		175 17 5	26 14 8
	100 3 5	„ Balance, being Excess of Income over Expenditure, carried to Balance Sheet		47 1 11
	£12,186 6 7			£12,821 18 11

Income and Expenditure Accounts of other Funds for the Year ended 31st December, 1944.

PUBLICATIONS FUND.

1943 £ s. d.	1943 £ s. d.	*Income.*	1944 £ s. d.	1944 £ s. d.
		To Publication Sales (including back numbers):		
2756 1 0		Journals and Proceedings	3140 3 9	
76 10 9		Collective Index	6 19 0	
594 13 3		Annual Reports on Progress of Chemistry ...	715 3 7	
139 8 6		Authors' Extra Reprints	115 1 10	
6 4 9		Other Publications	8 6 7	
	3572 18 3			3985 14 9
		„ Net Proceeds of Advertisements:		
742 7 5		Journal	742 16 4	
91 5 10		Annual Reports	71 11 10	
	833 13 3			814 8 2
		„ Donations:		
9 11 6		Fellows	10 10 0	
1000 0 0		Chemical Council	1000 0 0	
		„ „ for Summaries to Papers in		
50 0 0		Journal	50 0 0	
	1059 11 6			1060 10 0
		„ Government Publications Grant (through the		
	200 0 0	Royal Society		200 0 0
		„ Allocation from the Rockefeller Grant		
	500 0 0	(through the Royal Society)		500 0 0
		„ Cost of publishing Tilden Lectures:		
	12 12 0	Transfer from the Tilden Lecture Fund ...		25 4 0
	202 8 9	„ Dividends on Investments		202 15 10
	232 2 8	„ Income Tax recovered		211 17 9
		„ Transfer from General Purposes Account (the		
	6452 13 9	balance of expenditure on publications) ...		6261 12 9
	£13,066 0 2			£13,262 3 3

1943 £ s. d.	1943 £ s. d.	*Expenditure.*	1944 £ s. d.	1944 £ s. d.
		By Expenses on account of Journal:		
1173 0 0		Editorial Salaries	1207 8 7	
85 12 6		Superannuation	85 12 6	
18 10 5		Editorial Postages	17 16 2	
2884 0 3		Printing and Paper	3135 14 4	
510 9 10		Banding and Distribution	586 8 0	
342 10 9		Authors' Reprints	353 2 8	
9 19 11		Miscellaneous	10 4 3	
356 12 0		Overhead Expenses (proportion)	522 17 2	
44 18 11		War Damage Insurance	28 3 4	
	5425 14 7			5947 7 0
		„ Contributions to Bureau:		
		Balance of Expenditure on Abstracts A I		
1977 7 5		and A II	1906 19 11	
1500 0 0		Agreed amounts to Abstracts A III	1500 0 0	
		Contribution to Abstracts C (proportion of		
— — —		cost)	268 5 11	
	3477 7 5			3675 5 10
	3300 0 0	„ Transfer to Special Reserve Fund (including Quinquennial Index)		2700 0 0
	862 18 2	„ Annual Reports on the Progress of Chemistry Printing and Honoraria		939 10 5
	£13,066 0 2			£13,262 3 3

Income and Expenditure Accounts of other Funds for the Year ended 31st December, 1944.

LIBRARY.

1943 £ s. d.	1943 £ s. d.	*Income.*	1944 £ s. d.	1944 £ s. d.
		To Contribution for Fittings, Furniture, Books, Periodicals and Binding:		
850 9 4		Transfer from General Purposes Account ...	978 2 4	
— — —		„ „ Special Reserve Fund (deferred expenditure)	300 14 6	
		„ Air Raid Precautions:		
39 0 6		Transfer from General Purposes Account ...	27 5 6	
		„ War Damage Insurance:		
197 15 4		Transfer from General Purposes Account ...	119 10 9	
	1087 5 2			1425 13 1
		„ Contributions towards maintenance: *		
		Through the Chemical Council:		
		Chemical Society (transfer from General Purposes Account)	291 2 10	
346 8 4		Royal Institute of Chemistry	606 10 11	
721 13 10		Society of Chemical Industry	315 8 0	
375 5 7		From the Chemical Council	506 8 3	
250 0 0				
	1693 7 9			1719 10 0
		„ Contributions, etc., received from other sources towards maintenance:		
		Association of British Chemical Manufacturers	100 0 0	
100 0 0		Biochemical Society	21 0 0	
21 0 0		British Association of Chemists	50 0 0	
— — —		Faraday Society	26 5 0	
26 5 0		Institute of Brewing	50 0 0	
50 0 0		Society of Dyers and Colourists	10 10 0	
10 10 0		Society of Public Analysts and other Analytical Chemists	21 0 0	
21 0 0		Fellows	3 0 0	
3 0 0		Miscellaneous receipts	49 0 3	
20 7 6				
	252 2 6			330 15 3
	£3032 15 5			£3475 18 4

1943 £ s. d.	1943 £ s. d.	*Expenditure.*	1944 £ s. d.	1944 £ s. d.
		By Capital and Extraordinary Expenditure		
308 6 1		Books and Periodicals *	823 3 1	
42 3 3		Binding	55 13 9	
500 0 0		Transfer to Special Reserve Fund	400 0 0	
39 0 6		Air Raid Precautions	27 5 6	
197 15 4		War Damage Insurance	119 10 9	
	1087 5 2			1425 13 1
		„ Maintenance:		
1334 0 0		Salaries	1569 4 7	
95 15 5		Superannuation of Library Staff	120 7 4	
33 0 0		Postages	43 0 0	
14 6 7		Miscellaneous Expenses	15 4 9	
238 2 3		Overhead Expenses (proportion)	302 8 7	
	1715 4 3			2050 5 3
	230 6 0	„ Balance, amount transferred to General Purposes Account		— — —
	£3032 15 5			£3475 18 4

* Other than those received in exchange.

Income and Expenditure Accounts of other Funds for the Year ended 31st December, 1944.

SPECIAL RESERVE FUND.

1943	*Income.*	1944
£ s. d.		£ s. d.
120 3 7	To Dividends on Investments	175 5 3
13 0 6	„ Interest on Deposit at Bankers and in Post Office Savings Bank	18 17 4
59 9 5	„ Income Tax recovered	91 19 10
£192 13 6		£286 2 5

1943	*Expenditure.*	1944
£ s. d.		£ s. d.
192 13 6	By Balance, being Excess of Income over Expenditure, carried to Balance Sheet	286 2 5
£192 13 6		£286 2 5

RESEARCH FUND.

1943		1944
£ s. d.		£ s. d.
398 18 2	To Dividends on Investments	378 4 8
365 4 11	„ Income Tax recovered	365 4 11
57 7 6	„ Repayment of Grants	45 3 0
10 0 0	„ Grants not claimed	— — —
1 14 6	„ Interest on Deposit	18 9
1 2 7	„ Sale of Chemicals	— — —
£834 7 8		£789 11 4

1943		1944
£ s. d.		£ s. d.
177 0 0	By Grants	40 0 0
1 0 2	„ Miscellaneous Expenses	1 9 9
656 7 6	„ Balance, being Excess of Income over Expenditure, carried to Balance Sheet	748 1 7
£834 7 8		£789 11 4

SPECIAL PUBLICATIONS FUND.

£ s. d.	£ s. d.		£ s. d.	£ s. d.
		To Sales of Publications:		
8 16 0		Memorial Lecture, Vol. I	8 13 6	
9 6 5		„ „ Vol. II	7 18 1	
5 5 3		„ „ Vol. III	5 4 0	
2 15 8		Faraday Lectures	5 12 6	
		Portraits	1 8 11	
2 15 11		Other publications	1 15 4	
	28 19 3			30 12 4
	74 0 8	„ Dividend on Investment		74 0 8
	4 5 2	„ Interest on Deposit		4 16 7
	£107 5 1			£109 9 7

£ s. d.	*Expenditure.*	£ s. d.
107 5 1	By Balance, being Excess of Income over Expenditure, carried to Balance Sheet	109 9 7
£107 5 1		£109 9 7

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Income and Expenditure Accounts of other Funds for the Year ended 31st December, 1944.

CENTENARY FUND.

1943	*Income.*	1944	1943	*Expenditure.*	1944
£ s. d.		£ s. d.	£ s. d.		£ s. d.
26 0 0	To Interest on Deposit in Post Office Savings Bank and London Savings Bank	26 13 0	26 0 0	By Balance, being Excess of Income over Expenditure, carried to Balance Sheet	26 13 0
£26 0 0		£26 13 0	£26 0 0		£26 13 0

STAFF PENSIONS FUND.

£ s. d.		£ s. d.	£ s. d.		£ s. d.
300 0 0	To Transfer from General Purposes Account	900 0 0	130 0 0	By Pensions paid during 1944	130 0 0
66 6 7	„ Dividends on Investments	68 9 11		„ Balance, being Excess of Income over Expenditure, carried to Balance	
35 10 10	„ Income Tax recovered	35 10 11	271 17 5	Sheet	874 0 10
£401 17 5		£1004 0 10	£401 17 5		£1004 0 10

THE EDWARD FRANK HARRISON MEMORIAL TRUST FUND.

£ s. d.		£ s. d.	£ s. d.		£ s. d.
27 5 2	To Dividends on Investments	27 5 2	— — —	By Miscellaneous Expenses	3 5 4
25 2 0	„ Income Tax recovered	25 2 0		„ Balance, being Excess of Income over Expenditure, carried to Balance	
2 4	„ Interest on Deposit	10 0	52 9 6	Sheet	49 11 10
£52 9 6		£52 17 2	£52 9 6		£52 17 2

Income and Expenditure Accounts of other Funds for the Year ended 31st December, 1944

SPECIAL LECTURES FUND.

1943	*Income.*	1944	1943	*Expenditure.*	1944
£ s. d.		£ s. d.	£ s. d.		£ s. d.
33 18 4	To Dividends on Investments	33 18 4	25 0 0	By Honorarium	25 0 0
11 11 2	„ Income Tax recovered	11 11 2	— — —	„ Lecture Expenses	2 16 6
9 7	„ Interest on Deposit	13 6		„ Balance, being excess of Income over Expenditure, carried to Balance	
			20 19 1	Sheet	18 6 6
£45 19 1		£46 3 0	£45 19 1		46 3 0

THE FARADAY LECTURE FUND.

£ s. d.		£ s. d.	£ s. d.		£ s. d.
6 11 4	To Dividends on Investments	6 11 3		By Balance, being Excess of Income over Expenditure, carried to Balance	
6 11 3	„ Income Tax recovered	6 11 3	13 3 9	Sheet	13 7 6
1 2	„ Interest on Deposit	5 0			
£13 3 9		£13 7 6	£13 3 9		£13 7 6

THE TILDEN LECTURE FUND.

£ s. d.		£ s. d.	£ s. d.		£ s. d.
43 2 6	To Dividends on Investments	43 2 6	15 15 0	By Honoraria	47 5 0
30 11 0	„ Income Tax recovered	30 11 0	6 7 0	„ Lecture Expenses	9 19 3
4 2	„ Interest on Deposit	8 0	12 12 0	„ Transfer to Publications Fund, for cost of publication of Lectures... ...	25 4 0
	„ Balance, being Excess of Expenditure over Income, carried to Balance			„ Balance, being Excess of Income over Expenditure, carried to Balance	
— — —	Sheet	8 6 9	39 3 8	Sheet	— — —
£73 17 8		£82 8 3	£73 17 8		£82 8 3

THE CHEMICAL SOCIETY.—BALANCE SHEETS, 31st December, 1944.

GENERAL PURPOSES.

1943 £ s. d.	*Liabilities.*	£ s. d.	1944 £ s. d.
	To Subscriptions received in advance ...		2,978 14 11
1,670 16 11	„ Sundry Creditors (Printing and other Expenses)		7,110 19 10
4,341 12 11			2,700 0 0
3,000 0 0	„ Amount due to Special Reserve Fund...		
	„ Excess of Assets over Liabilities as per last Balance Sheet	21,493 9 4	
21,370 4 0	*Add* Life Composition Fees (£223 10*s.*)		
90 0 0	(two-thirds)	149 0 0	
33 1 11	*Add* Profit on realisation of investment	138 4 1	
	Add Excess of Income over Expenditure for year	47 1 11	
100 3 5			21,827 15 4
21,493 9 4			
£30,505 19 2			£34,617 10 1

1943 £ s. d.	*Assets.*	1944 £ s. d.
24,848 8 11	By Investments as per Schedule (cost or value when acquired)	24,986 13 0
2,255 13 9	„ Sundry Debtors	3,393 1 0
350 0 0	„ Subscriptions in Arrear (£707 19*s.* 0*d.*). Estimated to realise	350 0 0
— — —	„ Subscriptions in Suspense (£2,437 14*s.* 2*d.*)	— — —
308 0 9	„ Stock of Paper (Journal, Abstracts, and Annual Reports)	515 15 11
2,743 15 9	„ Cash in hand	5,372 0 2
£30,505 19 2		£34,617 10 1

THE CHEMICAL SOCIETY. BALANCE SHEETS, 31ST DECEMBER, 1944.

PUBLICATIONS FUND.

1943 £ s. d.	1943 £ s. d.	*Liabilities.*	1944 £ s. d.	1944 £ s. d.
10,363 3 10		To Excess of Assets over Liabilities as per last Balance Sheet	9564 5 9	
798 18 1		*Deduct* Loss on realisation of Investment	26 17 1	
	9564 5 9			9537 8 8
	£9564 5 9			£9537 8 8

1943 £ s. d.	1943 £ s. d.	*Assets.*	1944 £ s. d.	1944 £ s. d.
9564 5 9		By Investments as per Schedule (cost or value when acquired)		9537 8 8
	£9564 5 9			£9537 8 8

SPECIAL RESERVE FUND.

1943 £ s. d.	1943 £ s. d.		1944 £ s. d.	1944 £ s. d.
	— — —	To Sundry Creditor		300 14 6
		„ Reserve for Publications (including Quinquennial Index) as per last Balance Sheet	9400 0 0	
6400 0 0		*Add* Amount transferred from General Purposes Account	2700 0 0	
3000 0 0		*Add* Amount transferred from Quinquennial Index Fund	485 0 7	
— — —			12,585 0 7	
9400 0 0		*Less* Amount transferred to Bureau of Abstracts	175 0 0	
	9400 0 0			12,410 0 7
		„ Reserve for Library Books and Binding as per last Balance Sheet	1300 16 0	
800 16 0		*Add* Amount transferred from General Purposes Account	400 0 0	
500 0 0			1700 16 0	
1300 16 0		*Less* Amount transferred to General Purposes Account for Library Books	300 14 6	
— — —				1400 1 6
	1300 16 0			
		„ Reserve for Research Fund as per last Balance Sheet	2850 0 0	
2150 0 0		*Add* Amount transferred from Research Fund	500 0 0	
700 0 0				3350 0 0
	2850 0 0			
	100 0 0	„ Emile Mond Bequest as per last Balance Sheet		100 0 0
		„ Excess of Income over Expenditure brought forward	287 13 8	
95 0 2		*Add* Excess of Income over Expenditure for year	286 2 5	
192 13 6				573 16 1
	287 13 8			
	£13,938 9 8			£18,134 12 8

1943 £ s. d.	1943 £ s. d.	*Assets.*	1944 £ s. d.	1944 £ s. d.
9000 0 0		By Investments as per Schedule (cost or value when acquired)		12,700 0 0
3000 0 0		„ Sundry Debtors (General Purposes Account)		3,100 0 0
1414 5 0		„ Cash at Bank		992 5 10
524 4 8		„ Cash on Deposit in Post Office Savings Bank		1,342 6 10
	£13,938 9 8			£18,134 12 8

THE CHEMICAL SOCIETY. BALANCE SHEETS, 31ST DECEMBER, 1944.

RESEARCH FUND.

1943 £ s. d.	1943 £ s. d.	*Liabilities.*	1944 £ s. d.	1944 £ s. d.
	35 19 10	To Sundry Creditors		46 9 9
18,543 4 7		„ Excess of Assets over Liabilities as per last Balance Sheet	18,499 12 1	
656 7 6		*Add* Excess of Income over Expenditure for year	748 1 7	
19,199 12 1			19,247 13 8	
700 0 0		*Deduct* Amount transferred to Special Reserve Fund	500 0 0	
			18,747 13 8	
— — —		*Add* Profit on Realisation of Investment	231 6 2	
	18,499 12 1			18,978 19 10
	£18,535 11 11			£19,025 9 7

1943 £ s. d.	1943 £ s. d.	*Assets.*	1944 £ s. d.	1944 £ s. d.
18,377 9 5		By Investments as per Schedule (cost or value when acquired)		18,608 15 7
158 2 6		„ Cash at Bank and on deposit in Post Office Savings Bank		416 14 0
	£18,535 11 11			£19,025 9 7

SPECIAL PUBLICATIONS FUND.

£ s. d.	£ s. d.	*Liabilities.*	£ s. d.	£ s. d.
	11 1	To Sundry Creditors		1 16 5
2487 16 0		„ Excess of Assets over Liabilities as per last Balance Sheet	2595 1 1	
107 5 1		*Add* Excess of Income over Expenditure for year	109 9 7	
	2595 1 1			2704 10 8
	£2595 12 2			£2706 7 1

£ s. d.	£ s. d.	*Assets.*	£ s. d.	£ s. d.
1600 0 0		By Investment as per Schedule (cost or value when required)		1600 0 0
995 12 2		„ Cash at Bank and on Deposit in the Post Office Savings Bank and London Savings Bank		1106 7 1
	£2595 12 2			£2706 7 1

THE CHEMICAL SOCIETY. BALANCE SHEETS, 31ST DECEMBER, 1944.

CENTENARY FUND.

1943 £ s. d.	1943 £ s. d.	*Liabilities.*	1944 £ s. d.	1944 £ s. d.	1943 £ s. d.	1943 £ s. d.	*Assets.*	1944 £ s. d.
1052 1 8		To Excess of Assets over Liabilities as per last Balance Sheet	1078 1 8		10 15 6		By Cash at Bank	10 15 6
26 0 0		*Add* Excess of Income over Expenditure for year	26 13 0		1067 6 2		„ Cash on Deposit in Post Office Savings Bank and London Savings Bank	1093 19 2
	1078 1 8			1104 14 8				
	£1078 1 8			£1104 14 8	£1078 1 8			£1104 14 8

STAFF PENSIONS FUND.

£ s. d.	£ s. d.		£ s. d.	£ s. d.	£ s. d.	£ s. d.		£ s. d.
	12 10 0	To Sundry Creditors		12 10 0	— — —		By Sundry Debtor	900 0 0
3368 12 8		„ Excess of Assets over Liabilities as per last Balance Sheet	3640 10 1		3322 13 9		„ Investments as per Schedule (cost or value when acquired)	3619 10 10
271 17 5		*Add* Excess of Income over Expenditure for year	874 0 10		330 6 4		„ Cash at Bank	4 7 2
3640 10 1			4514 10 11					
— — —		*Deduct* Loss on Realisation of Investment	3 2 11					
	3640 10 1			4511 8 0				
	£3653 0 1			£4523 18 0	£3653 0 1			£4523 18 0

THE EDWARD FRANK HARRISON MEMORIAL TRUST FUND.

£ s. d.	£ s. d.		£ s. d.	£ s. d.	£ s. d.	£ s. d.		£ s. d.
1156 9 6		To Excess of Assets over Liabilities as per last Balance Sheet	1208 19 0		1101 7 11		By Investments as per Schedule (cost or value when acquired)	1101 7 11
52 9 6		*Add* Excess of Income over Expenditure for year	49 11 10		107 11 1		„ Cash at Bank	157 2 11
	1208 19 0			1258 10 10				
	£1208 19 0			£1258 10 10	£1208 19 0			£1258 10 10

THE CHEMICAL SOCIETY. BALANCE SHEETS, 31ST DECEMBER, 1944.

SPECIAL LECTURES FUND.

1943 £ s. d.	1943 £ s. d.	*Liabilities.*	1944 £ s. d.	1944 £ s. d.	1943 £ s. d.	1943 £ s. d.	*Assets.*	1944 £ s. d.	1944 £ s. d.
1168 18 6		To Excess of Assets over Liabilities as per last Balance Sheet	1189 17 7		1000 0 0		By Investment as per Schedule (cost or value when acquired)	1000 0 0	
20 19 1		*Add* Excess of Income over Expenditure for year	18 6 6		189 17 7		„ Cash at Bank	208 4 1	
	1189 17 7			1208 4 1					
	£1189 17 7			£1208 4 1	£1189 17 7				£1208 4 1

THE FARADAY LECTURE FUND.

£ s. d.	£ s. d.		£ s. d.	£ s. d.	£ s. d.	£ s. d.		£ s. d.	£ s. d.
418 11 0		To Excess of Assets over Liabilities as per last Balance Sheet	431 14 9		369 4 0		By Investment as per Schedule (cost or value when acquired)	369 4 0	
13 3 9		*Add* Excess of Income over Expenditure for year	13 7 6		62 10 9		„ Cash at Bank	75 18 3	
	431 14 9			445 2 3					
	£431 14 9			£445 2 3	£431 14 9				£445 2 3

THE TILDEN LECTURE FUND.

£ s. d.	£ s. d.		£ s. d.	£ s. d.	£ s. d.	£ s. d.		£ s. d.	£ s. d.
	12 12 0	To Sundry Creditors		12 12 0	1878 14 10		By Investments as per Schedule (cost or value when acquired)	1878 14 10	
1939 19 1		„ Excess of Assets over Liabilities as per last Balance Sheet	1979 2 9		112 19 11		„ Cash at Bank	104 13 2	
89 3 8		*Add* Excess of Income over Expenditure for year							
— — —		*Deduct* Excess of Expenditure over Income for year	8 6 9						
	1979 2 9			1970 16 0					
	£1991 14 9			£1983 8 0	£1991 14 9				£1983 8 0

SCHEDULE OF INVESTMENTS.

GENERAL PURPOSES.

Nominal Details.	*Cost or Value when Acquired.* £ s. d.	*Market Value 31st December 1944.* £ s. d.
£11,426 15s. 0d. 3½% Conversion Stock, 1961, or after	8874 2 2	12,112 7 1
£600 4% Funding Stock, 1960/90	480 0 0	681 0 0
£408 2s. 6d. 3% Funding Stock, 1959/69	394 11 5	410 3 4
£100 3% Savings Bonds, 1955/65	100 0 0	101 10 0
£1200 14s. 9d. 3% Savings Bonds, 1960/70	1200 14 9	1206 14 10
£3825 1s. 6d. Local Loans, 3%	3629 6 9	3614 13 11
£1520 14s. 3d. Cardiff Corporation 3% Stock, 1914/54	1650 0 0	1535 18 4
£2400 Bristol Corporation 2½% Debenture Stock, 1957	2070 2 0	2304 0 0
£1200 Leeds Corporation 3% Stock	1143 1 0	1128 0 0
£787 London, Midland and Scottish Railway 4% Debenture Stock	839 3 7	849 19 2
£2713 London, Midland and Scottish Railway 4% Preference Stock	3572 0 4	2143 5 5
£1200 London and North Eastern Railway 3% Debenture Stock...	1033 11 0	1026 0 0
	£24,986 13 0	£27,113 12 1

PUBLICATIONS FUND.

£5260 19s. 9d. 3½% Conversion Stock, 1961, or after	3645 12 8	5576 12 11
£1000 3% Savings Bonds, 1955/65	1000 0 0	1015 0 0
£1261 1s. 11d. 3% Savings Bonds, 1960/70	1261 1 11	1267 8 0
£3344 3s. 4d. Local Loans 3%	3173 1 6	3160 4 9
£603 London, Midland and Scottish Railway 4% Guaranteed Stock	457 12 7	636 3 4
	£9537 8 8	£11,655 9 0

RESEARCH FUND.

£10,177 16s. 1d. 3½% Conversion Stock, 1961, or after	8833 2 3	10,788 9 5
£4741 4s. 10d. Local Loans, 3%	4498 11 0	4480 9 5
£806 Victoria 3% Stock, 1929/49	706 6 2	806 0 0
£1000 London and North Eastern Railway 4% 2nd Guaranteed Stock	1010 0 0	935 0 0
£1034 Great Western Railway 2½% Debentures	1049 15 11	770 6 7
£1483 London, Midland and Scottish Railway 4% Debenture Stock	1508 3 6	1601 12 10
£1122 Metropolitan Water Board 3% "B" Stock	1002 16 9	1099 11 2
	£18,608 15 7	£20,481 9 5

SPECIAL RESERVE FUND.

£1000 3% National Defence Bonds	1000 0 0	1000 0 0
£2447 7s. 10d. 2½% National War Bonds, 1946/48	2450 0 0	2493 5 7
£1612 10s. 2d. 2½% National War Bonds, 1945/47	1650 0 0	1634 13 7
£2400 2½% National War Bonds, 1949/51	2400 0 0	2418 0 0
£3700 2½% National War Bonds, 1952/54	3700 0 0	3718 10 0
£1500 3% Savings Bonds, 1955/65	1500 0 0	1507 10 0
	£12,700 0 0	£12,771 19 2

SPECIAL PUBLICATIONS FUND.

Nominal Details.	*Cost or Value when Acquired.* £ s. d.	*Market Value 31st December, 1944.* £ s. d.
£2115 8s. 10d. 3½% Conversion Stock, 1961, or after	£1600 0 0	£2242 7 4

STAFF PENSIONS FUND.

£683 6s. 1d. 3½% Conversion Stock, 1961, or after	527 13 9	724 6 1
£2100 2½% National War Bonds, 1946/48	2100 0 0	2139 7 6
£150 2½% National War Bonds, 1951/53	150 0 0	151 2 6
£170 3% Savings Bonds, 1955/65	170 0 0	172 11 0
£300 3% Savings Bonds, 1960/70	300 0 0	301 10 0
£391 17s. 4d. Local Loans, 3%	371 17 1	370 6 3
	£3619 10 10	£3859 3 4

THE EDWARD FRANK HARRISON MEMORIAL TRUST FUND.

£61 15s. 8d. 3½% Conversion Stock, 1961, or after	50 1 5	65 9 9
£1255 London, Midland and Scottish Railway 4% Debenture Stock	1051 6 6	1355 8 0
	£1101 7 11	£1420 17 9

SPECIAL LECTURES FUND.

£1299 9s. 4d. 3½% Conversion Stock 1961 or after	£1000 0 0	£1377 8 8

THE FARADAY LECTURE FUND.

£374 19s. 0d. 3½% Conversion Stock, 1961, or after...	£369 4 0	£397 8 11

THE TILDEN LECTURE FUND.

£419 4s. 10d. 3% Funding Stock, 1959/69	386 12 10	421 6 9
186 National Provincial Bank Shares £5 each, £1 paid "B"... ...	678 18 0	720 15 0
£532 London Transport "B" 5% Stock	625 2 0	651 14 0
£220 Metropolitan Water Board (Kent Water Works) 3% Deb. Stock	188 2 0	205 14 0
	£1878 14 10	£1999 9 9

F. P. DUNN, *Treasurer.*

We have examined the above Balance Sheets and accompanying Income and Expenditure Accounts with the Books and Vouchers of the Society, and certify them to be in accordance therewith. We have also verified the Balances at the Bankers and the Investments.

224, REGENT STREET, W. 1.
16th May, 1945.

W. B. KEEN & Co.
Chartered Accountants.

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APPENDIX A.

REPORT OF THE BUREAU OF CHEMICAL AND PHYSIOLOGICAL ABSTRACTS FOR THE YEAR 1944.

1. *Title and Incorporation.*

This is the last report to be issued by the Bureau under the name which it assumed in 1938, when the sphere of activity was increased from the purely chemical field to include more specifically both physiology and biochemistry. Since that time further widening has taken place; for example, the Anatomical Society joined the Bureau in 1939 and the Society for Experimental Biology in 1944, and in view of other possible developments, it was decided to assume (with the full approval of the supporting bodies) a more general name—the Bureau of Abstracts. It is under this name that the Bureau has sought, as mentioned in last year's report, incorporation. This matter, the legal aspect in particular, has been pressed forward, and it had been hoped that it would have been possible to report by the end of 1944 that incorporation had been effected Although the present report is for the year 1944, it may be stated that early in 1945 the necessary legal steps were completed.

2. *Criticisms of Bureau Publications.*

The Bureau deplores the limitations imposed by War on its activities and is acutely conscious of the improvements so urgently desired by the chemical community. Criticisms have been made, some of them, particularly in the Applied field, without full knowledge of the facts, some almost cancelling out, *e.g.*, that the Abstracts are too short and that the Abstracts are not concise enough. The Bureau welcomes criticism. The more important reasons for dissatisfaction put forward may be roughly grouped as follows:

(*a*) That British Abstracts are redundant—only one set of abstracts in the English language should be published.
(*b*) That the " spread " of abstracts published by the Bureau is not sufficiently wide.
(*c*) That the publications are not worthy of the Bureau (they should be better printed with larger margins; they should not be rolled up for despatch, etc.).
(*d*) That the present use of abbreviations should be reduced materially.
(*e*) That the Index is in need of improvement.

The Bureau during the year under review has considered these points among many others.

The first criticism is of far-reaching importance, and cannot be ignored. The preparation and publication of only one set of chemical abstracts in the English language instead of two should lead to economy of effort and possibly to all-round economy. It must be pointed out that attempts have been made in the past to co-operate with the American Chemical Society in the production of abstracts, the last as recently as during the past year, but there are difficulties. It is not at all certain that the majority of British chemists would prefer the American method of publication to our own, and although it might be possible to arrange to leave the publication of chemical abstracts entirely to the American Chemical Society, this is a step which the Bureau does not at present contemplate. Measures of co-operation will, however, continue to be explored.

There is one other very important consideration. The Abstracts published by the American Chemical Society are not the only ones issued in the States; those of the Bureau are not the only ones issued in Great Britain. It would appear obvious that integration on a national scale both in America and Great Britain would make international agreement more possible. In this connexion it is of importance to record that during the year a joint Committee of the Bureau and of Science Abstracts has been set up to explore possible co-operation, and as a result some valuable mutual help has been given and received.

It is evident that in spite of criticisms the publications of the Bureau are necessary, otherwise there would not be the continual increase in outside subscriptions.

The second criticism also demands careful consideration.

In the first place, the Bureau is handicapped by the difficulty of obtaining the original journals, for whereas before the War some 1000 were abstracted, to-day the total number is only 530. It is definitely the intention of the Bureau to improve on the 1938 standard, but there is a point which is often forgotten, namely, that as the scope of Abstracts increases so the appeal to more groups of specialists increases,

and it will be the policy of the Bureau to try to satisfy this continually expanding demand. It is, however, obvious that there will be much leeway to recover when more journals issued during War-time become available.

Another criticism of a similar nature to the preceding is that Abstracts should not be issued in sections, but as one publication, as are American Abstracts. Some of the critics appear to forget that there is nothing to prevent anyone having *all* the sections—in fact many subscribers do so. The present method of issue, however, has two advantages: during war-time it has permitted a considerable saving in paper and it has anticipated and met the needs of the critics who complained that they were only interested in a special branch and did not want to pay for the whole of the Abstracts. The Bureau is, however, giving consideration to another aspect of publication, namely, the arbitrary division into A and B Groups, representing Pure and Applied Chemistry, a legacy of the days when "A" Abstracts were published by the Chemical Society and "B" Abstracts by the Society of Chemical Industry. Many would like to see this separation abolished.

The criticisms under paragraph (*c*) above show a lack of appreciation of the limitations imposed by War conditions. Immediate steps will be taken to remedy these defects as soon as conditions allow.

When paper supply permits, it is the intention to revert to the publication of one joint index. Moreover, a special Committee is now sitting to discuss the whole question of indexing, including the possibility of publication of a formula index and of other specialised indexes.

The final criticism listed above is still receiving serious consideration. It is admitted that the Abstracts suffer by reason of excessive use of abbreviations and contractions introduced to save space. A Bureau committee is to report shortly on this matter.

The year has witnessed in spite of all shortcomings an increased sale of all sections of Abstracts to non-members of the supporting Societies, especially of A III.

3. *Progress of Section C.*

The most important change that has been made in the Abstracts since 1938 was introduced during the year with the issue of Section C (Analysis and Laboratory Apparatus). This Section provides a comprehensive collection of all abstracts on these subjects which had previously been scattered about throughout the other Sections and were not therefore accessible to those who did not take all the publications of the Bureau. Section C is for the present distributed without extra charge to all members who wish to receive it, and is available to non-members at 15*s.* per annum, complete with its own index. Four quarterly issues were published during the year, covering 104 pages and containing 2086 abstracts. The first two issues were similar in arrangement to the other Sections in that they included cross-references to abstracts in Sections A and B in which the interest from the analytical or apparatus point of view was subsidiary to the main theme. It was decided, however, that the value of the Section would be much enhanced if it were made self-contained, and consequently in the later issues these cross-references were replaced by abstracts. The Bureau believes that, despite some inevitable duplication, this is a progressive step and one which may possibly be extended to Sections A and B as and when circumstances permit. To facilitate reading C Abstracts are classified—not too finely—into four groups:

I. Inorganic, Pure and Applied.
II. Organic, Pure and Applied.
III. Physiology; Biochemistry; Foods; Sanitation; Agriculture.
IV. General Technique and Laboratory Apparatus.

A great part of its success has been due to the enthusiastic work of Dr. E. B. Hughes as its Assistant Editor; he has had the collaboration of a virile Sub-Committee consisting of Mr. R. C. Chirnside, Mr. B. S. Cooper, Dr. E. J. King, and Dr. A. Parker, which at its quarterly meetings reviews the proofs of the forthcoming issue in detail. The expenses of the C Abstracts are allocated on the basis of the number of abstracts in C which would formerly have appeared in the various other Sections. The proportion for 1944 was A I and A II 34%; A III 22%; B 44%.

4. *Society for Experimental Biology.*

The Bureau welcomes the addition as mentioned above of the Society for Experimental Biology to the list of contributing Societies. This Society makes an annual contribution to the funds of the Bureau, and its members receive Section A III at a preferential rate. Two of the members of the Society for Experimental Biology, viz. Dr. L. G. G. Warne and Dr. G. P. Wells, are assisting the editorial staff of A III in their special fields.

5. Finance.

The expenditure and income of the Bureau for the year under review can be summarised as follows :

Expenditure.			Income.		
1943.		1944.	1943.		1944.
£		£	£	£	£	£
	Cost of Production :			Sales and Advertisements :		
2010	A I	2174	2217	A I and A II	2708	
2245	A II	2441	2195	A III	3197	
3928	A III	4202	2733	B I, B II and B III	3059	
2493	B I	2408	—	C	46	
2087	B II	2245	——	7145	——	9010
1690	B III	1705		Contributions :		
—	C	835	3477	Chemical Society	3675	
			3609	Society of Chemical Industry	3721	
			400	Physiological Society	400	
			300	Biochemical Society	300	
			100	Anatomical Society	100	
			—	Society of Experimental Biology	50	
			380	Chemical Council	2466	
			97	Miscellaneous	6	
			——	8363	——	10,718
				15,508		19,728
				1055	*Less* Transferred to Reserve and Balance	3718
£14,453		£16,010		£14,453		£16,010

The expenditure is £1557 more than last year, an increase to be attributed to the production of Section C (£835) and increase in the actual costs of printing, paper, etc., for it will be noted from Appendix II that the number of pages printed and also the number of abstracts show slight reductions in comparison with 1943.

This increase in expenditure is, however, more than offset by the increase in revenue from sales and advertisements, which are £1865 higher than the previous year. It will be understood that these sales are to non-members of the contributing societies and are therefore a definite indication of the growing interest in the publications of the Bureau. Sales in all sections, as the figures reveal, show an increase, the most marked being in A III, sales of which exceeded those for 1943 by £1002. This notable increase can only be interpreted as a very clear expression of the esteem in which Section A III is held. The Bureau considers that this is due in a very large measure to the outstanding editorial service of Professor Samson Wright and Dr. J. H. Birkinshaw and their team of specialist advisers.

The contributions to the Bureau by the Chemical Society and by the Society of Chemical Industry are respectively £3675 and £3721, figures which, notwithstanding the increase of sales, are greater than in 1943, largely due to the issue of Section C. Once again £1500 has been contributed by the Chemical Society to the A III account (so that their contribution to A I and A II is £2175). £75 has been contributed by the Society of Chemical Industry and £466 by the Chemical Council in respect of A III abstracts to members under the conjoint scheme. The Bureau, however, wishes very gratefully to acknowledge a gift of £2000 from the Chemical Council, and has expressed its great appreciation of this recognition of its work. In this connection it is germane to quote from "An Appeal to Industry" issued by the Chemical Council in March, 1944.

"Even now, when the increased costs of publication have been practically off-set by the limitation of paper, the Bureau would be able, with more funds at its disposal, to improve its abstracting service.

"The greater the sphere of activity of the Bureau the greater will be the economies to be effected in abstracting, and this is becoming possible particularly in view of the fact that the Bureau has improved its publication of abstracts progressively during the past decade.

"When the present conflict is over it is unlikely that the publishing societies will, unaided, be able to publish and abstract much more than a half of the material available, and chemists, who bore the whole burden of this task for so many years prior to 1936 until it became too heavy for them, must, and do, look to industry, which derives so much from their services, for considerable financial support.

"It must also be remembered that, immediately the present hostilities cease, there will be an enormous amount of new matter to be published, and, as this will occur not only in this country but throughout the world, the call on our abstracting services will likewise be very greatly increased."

The Bureau has opened a special Reserve Fund and to this has placed the £2000. The reserve fund for A III has been increased by £2550 and now stands at £3983.

Sales of the Collective Indexes published by the Bureau continue at a steady rate, and refunds have been made to the Chemical Society and the Society of Chemical Industry of £50 each for receipts from the Decennial Index (1923—1932) and £85 each for the Quinquennial Index (1933—1937).

6. *General.*

Two changes have taken place in the membership of the Bureau during the year. Dr. G. L. Brown (Physiological Society) and Prof. C. W. Davies (Chemical Society) have resigned; they were replaced by Professor Samson Wright and Professor G. M. Bennett respectively.

In April the Bureau decided that it was desirable to have a Vice-Chairman, and the choice fell unanimously on Professor B. A. McSwiney, who has been a most enthusiastic representative of the Physiological Society on the Bureau since the joint agreement was made in 1937 and has also been a valuable member of the Finance Committee from its commencement in 1939.

The first meeting of the Bureau under its original title took place on November 19th, 1923, and the congratulations of the present Bureau were at the appropriate meeting offered to Mr. Julian Baker and the Editor, Mr. Burton, who for 21 years have so ably supported the work.

The title of Section A III of the Abstracts has been slightly altered, so that now it is "Physiology, Biochemistry, Anatomy."

The Bureau has appointed Sub-Committees for Sections A I, A II, and B to examine and report on means whereby abstracts in these Sections may be improved.

The number of abstracts printed continues to show a small decrease, the figures being 23,119 in 1944 as compared with 25,195 in 1943 (see Appendix II). This decrease is distributed approximately equally among all the Sections when account is taken of the number of abstracts now appearing in Section C. No material increase in these figures can be anticipated until further supplies of paper become available.

In conclusion, the Bureau again expresses its cordial thanks to the Assistant Editors and Abstractors, who have continued to give such loyal service under difficult conditions, and also to the various Libraries which have so generously loaned journals for abstracting.

Appendix II.

The figures given in the appended Table show the number of abstracts and pages printed in each Section during 1944, together with comparative figures for 1943.

	1943.		1944.	
	No. Abs.	Pages.	No. Abs.	Pages.
A I	3149	162	2472	148
A II	1639	202	1466	192
A III	8992	464	7554	428
B I	5254	254	4020	210
B II	3520	200	3124	192
B III	2641	154	2417	134
C	—	—	2086	104
	25,195	1436	23,139	1408

Appendix I.

BUREAU OF CHEMICAL AND PHYSIOLOGICAL ABSTRACTS.

Income and Expenditure Account of Abstracts A I and A II for the Year ended 31st December, 1944.

1943	*Expenditure.*			1944		
£ s. d.		£ s. d.	£ s. d.	£ s. d.	£ s. d.	
	Abstracts A I:					
383 16 0	To Editorial Salaries	393 15 7				
22 9 9	„ Postages	24 19 2				
242 10 5	„ Abstractors' Fees	224 14 11				
678 4 8	„ Printing and Paper	741 17 5				
145 11 11	„ Banding and Distribution ...	170 6 9				
49 5 9	„ Miscellaneous (including War Damage Insurance)	51 19 3		1607 13 1		
1521 18 4						
	„ Index—					
64 0 8	Salaries	73 5 11				
4 12 1	Superannuation	4 12 9				
181 13 9	Printing and Paper	193 15 3				
20 4 2	Banding and Distribution ...	22 7 5				
3 7 4	Miscellaneous	7 2 7		301 3 11		
273 18 0						
147 13 0	„ Share of Overhead Expenses, The Chemical Society	213 19 2				
65 6 8	„ Share of Overhead Expenses, Society of Chemical Industry	51 13 4		265 12 6		
212 19 8					2174 9 6	
2008 16 0						
	Abstracts A II:					
316 16 8	To Editorial Salaries	335 8 0				
23 7 3	„ Postages	26 5 8				
302 7 10	„ Abstractors' Fees	290 13 6				
913 7 4	„ Printing and Paper	949 2 6				
145 11 11	„ Banding and Distribution ...	170 6 9				
49 5 8	„ Miscellaneous (including War Damage Insurance)	51 19 3		1823 15 8		
1750 16 8						
	„ Index—					
79 17 0	Salaries	94 10 3				
4 12 1	Superannuation	4 12 8				
172 2 0	Printing and Paper	219 0 6				
21 17 0	Banding and Distribution ...	23 19 6				
4 3 11	Miscellaneous	9 3 11		351 6 10		
282 12 0						
147 13 0	„ Share of Overhead Expenses, The Chemical Society	213 19 2				
65 6 8	„ Share of Overhead Expenses, Society of Chemical Industry	51 13 4		265 12 6		
212 19 8					2440 15 0	
2246 8 4						
£4255 4 4					£4615 4 6	

1943	*Income.*	1944	
£ s. d.		£ s. d.	£ s. d.
2217 4 11	By Sales of Abstracts A I and A II	2652 1 11	
60 12 0	„ Net Revenue from Advertisements	56 2 8	
1977 7 5	„ Transfer from The Chemical Society Publications Fund (the balance of Expenditure on Abstracts A I and A II)	1906 19 11	
£4255 4 4			£4615 4 6

Income and Expenditure Account of Abstracts A III for the Year ended 31st December, 1944.

1943 £ s. d.	1943 £ s. d.	*Expenditure.*	1944 £ s. d.	1944 £ s. d.
557 4 6		To Editorial Salaries	587 13 6	
27 6 5		„ Postages	25 10 2	
699 14 10		„ Abstractors' Fees	639 2 4	
1563 9 0		„ Printing and Paper	1610 14 7	
145 1 2		„ Banding and Distribution	168 5 0	
30 12 10		„ Miscellaneous (including War Damage Insurance)	35 7 1	
	3023 8 9			3066 12 8
		„ Index :		
183 8 2		Editorial Salaries	210 17 7	
11 14 8		Superannuation	11 13 5	
465 15 9		Printing and Paper	603 16 5	
21 1 11		Banding and Distribution	22 5 2	
9 12 9		Miscellaneous	20 10 4	
	691 13 3			869 2 11
147 13 0		„ Share of Overhead Expenses, Chemical Society	213 19 1	
65 6 8		„ Share of Overhead Expenses, Society of Chemical Industry	51 13 4	
	212 19 8			265 12 5
		„ Contribution to Abstracts C (proportion of cost)		173 11 9
	950 0 0	„ Transfer to Reserve Fund		1700 0 0
	105 2 6	„ Excess of Income over Expenditure, carried to Balance Sheet		18 15 10
	£4983 4 2			£6093 15 7

1943 £ s. d.	1943 £ s. d.	*Income.*	1944 £ s. d.	1944 £ s. d.
	2195 3 5	By Sales of Abstracts A III		3168 12 5
		„ Contributions :		
1500 0 0		The Chemical Society (Annual Grant)	1500 0 0	
400 0 0		The Physiological Society	400 0 0	
300 0 0		The Biochemical Society	300 0 0	
100 0 0		The Anatomical Society	100 0 0	
75 0 0		The Society of Chemical Industry	75 0 0	
380 0 0		The Chemical Council	466 0 0	
		The Society for Experimental Biology	50 0 0	
	2755 0 0			2891 0 0
	2 14 9	„ Interest on Deposit		6 1 9
	30 6 0	„ Net Revenue from Advertisements		28 1 5
	£4983 4 2			£6093 15 7

Balance Sheet of Abstracts A III, 31st December, 1944.

£ s. d.	£ s. d.	*Liabilities.*	£ s. d.	£ s. d.
	1469 0 2	To Sundry Creditors		1972 10 11
	950 0 0	„ Amount due to Reserve Fund		1700 0 0
177 3 11		„ Excess of Assets over Liabilities as per last Balance Sheet	277 6 5	
105 2 6		*Add* Excess of Income over Expenditure for year	18 15 10	
	277 6 5			296 2 3
	£2696 6 7			£3968 13 2

£ s. d.	£ s. d.	*Assets.*	£ s. d.	£ s. d.
1225 4 4		By Sundry Debtors		2045 1 10
1471 2 3		„ Cash at Bank		1923 11 4
	£2696 6 7			£3968 13 2

Income and Expenditure Account of Abstracts A III Reserve Fund, 31st December, 1944.

1943	*Expenditure.*	1944
£ s. d.		£ s. d.
28 11 6	To Excess of Income over Expenditure carried to Balance Sheet	47 17 0
£28 11 6		£47 17 0

1943	*Income.*	1944
£ s. d.		£ s. d.
28 11 6	By Dividend on Investments	33 17 0
— — —	„ Income Tax recovered	14 0 0
£28 11 6		£47 17 0

Balance Sheet of Abstracts A III Reserve Fund, 31st December, 1944.

Liabilities.						*Assets.*					
£ s. d.	£ s. d.		£ s. d.	£ s. d.		£ s. d.	£ s. d.		£ s. d.	£ s. d.	
1405 3 0		To Excess of Assets over Liabilities as per last Balance Sheet	2383 14 6			1400 0 0		By Investments as per Schedule (cost or value when acquired)	2350 0 0		
		Add Amount transferred from Abstract A III Account	1700 0 0			12 0 11		„ Sundry Debtors	— — —		
950 0 0						950 0 0		„ Amount due from A III Account	1700 0 0		
		Add Excess of Income over Expenditure for year	47 17 0			21 13 7		„ Cash at Bank	81 11 6		
28 11 6											
	2383 14 6			4131 11 6							
	£2383 14 6			£4131 11 6		£2383 14 6				£4131 11 6	

Schedule of Investments of Abstracts A III Reserve Fund.

	Value or Cost when Acquired.	Market Value 31st December, 1944.
	£ s. d.	£ s. d.
£700 3% Savings Bonds, 1955/65	700 0 0	710 10 0
£700 2½% National War Bonds, 1951/53	700 0 0	705 5 0
£900 2½% National War Bonds, 1952/54	950 0 0	954 15 0
	£2350 0 0	£2370 10 0

F. P. Dunn, *Treasurer of Bureau.*

We have examined the above Balance Sheets and accompanying Income and Expenditure Accounts with the Books and Vouchers, and certify them to be in accordance therewith. We have also verified the Balances at the Bankers and the Investments.

224, Regent Street, W. 1.
16th May, 1945.

W. B. Keen & Co.,
Chartered Accountants.

Balance Sheet of Bureau of Chemical and Physiological Abstracts General Reserve Fund, 31st December, 1944.

Liabilities.		*Assets.*	
	£ s. d.		£ s. d.
To Excess of Income over Expenditure for year	2000 0 0	By Sundry Debtor	2000 0 0

BUREAU OF CHEMICAL AND PHYSIOLOGICAL ABSTRACTS.

Income and Expenditure Account of Abstracts B I, B II and B III for the Year ending 31st December, 1944.

1943 £ s. d.	1943 £ s. d.	*Expenditure.*	1944 £ s. d.	1944 £ s. d.	1944 £ s. d.
		Abstracts B I:			
438 3 3		To Editorial Salaries	425 3 6		
17 17 4		„ Postages	19 10 11		
382 4 2		„ Abstractors' Fees	316 9 3		
992 19 3		„ Printing and Paper	922 7 5		
129 6 10		„ Banding and Distribution ...	128 12 4		
19 11 11		„ Miscellaneous	28 14 4		
	1980 2 9			1840 17 9	
		„ Index—			
100 8 0		Salaries	103 10 3		
252 18 2		Printing and Paper	320 16 9		
29 5 2		Banding and Distribution ...	20 15 11		
5 5 7		Miscellaneous	10 1 5		
	387 16 11			455 4 4	
	125 6 8	„ Share of Overhead Expenses ...		111 13 4	
	2493 6 4				2407 15 5
		Abstracts B II:			
345 0 1		To Editorial Salaries	388 5 1		
17 17 4		„ Postages	19 10 11		
300 19 0		„ Abstractors' Fees	286 6 3		
843 16 10		„ Printing and Paper	909 5 0		
129 6 10		„ Banding and Distribution ...	128 12 3		
19 11 11		„ Miscellaneous	28 14 4		
	1656 12 0			1760 13 10	
		„ Index—			
79 1 2		Salaries	94 10 3		
199 1 2		Printing and Paper	252 10 7		
23 0 5		Banding and Distribution ...	16 7 4		
4 3 1		Miscellaneous	9 3 11		
	305 5 10			372 12 1	
	125 6 8	„ Share of Overhead Expenses ...		111 13 4	
	2087 4 6				2244 19 3
		Abstracts B III:			
265 13 1		To Editorial Salaries	271 11 3		
17 17 3		„ Postages	19 10 11		
231 14 8		„ Abstractors' Fees	198 5 6		
664 16 11		„ Printing and Paper	667 15 5		
129 6 10		„ Banding and Distribution ...	128 12 3		
19 11 11		„ Miscellaneous	28 14 4		
	1329 0 8			1314 9 8	
		„ Index—			
60 17 5		Salaries	66 4 5		
153 1 5		Printing and Paper	194 3 10		
17 14 0		Banding and Distribution ...	12 11 8		
3 4 0		Miscellaneous	6 8 10		
	234 16 10			279 8 9	
	125 6 8	„ Share of Overhead Expenses ...		111 13 4	
	1689 4 2				1705 11 9
	£6269 15 0				£6358 6 5

1943 £ s. d.	1943 £ s. d.	*Income.*	1944 £ s. d.	1944 £ s. d.
2732 16 9		By Sales of Abstracts	3056 17 5	
3 2 5		„ Share of Fees and Sundry Sales	2 11 4	
	2735 19 2			
	3533 15 10	„ Excess of Expenditure over Income transferred to Society of Chemical Industry ...	3298 17 8	
				6358 6 5
	£6269 15 0			£6358 6 5

Income and Expenditure Account of Abstracts C for the Year ended 31st December, 1944.

	£ s. d.		£ s. d.
To Editorial Salaries	11 16 9	By Sales of Abstracts C	45 14 0
„ Abstractors' Fees	154 10 3	„ Excess of Expenditure over Income transferred from:	
„ Printing and Paper	554 9 3	The Chemical Society	268 5 11
„ Banding and Distribution	113 19 4	The Society of Chemical Industry	347 3 11
		Abstracts A III Account	173 11 9
			789 1 7
	£834 15 7		£834 15 7

APPENDIX B.

ANNUAL REPORT OF THE JOINT LIBRARY COMMITTEE, 1944.

The inconveniences caused by long-range aerial attacks had no adverse effect on the use of the Library, for every activity again shows a marked increase. There were 1,095 more attendances by readers than in 1943, and books borrowed increased by 761, postal loans accounting for 263 of this increase.

Telephone enquiries numbered 1,527, an increase of 110 on the previous year, whilst photostat copying again showed a considerable expansion, 3,687 pages being copied, against 2,873 last year. To this must be added 138 pages which were microfilmed, and from which a positive roll enlargement was supplied.

Additions to the Library consisted of 213 books, of which 42 were presented, 455 volumes of periodicals, and 146 pamphlets. The Library now contains 46,273 volumes, of which 13,809 are books and 32,464 volumes of periodicals.

Analysis.

	Attendances.	Books borrowed.	Books added.	Volumes of periodicals.	Pamphlets.
1944	7787	7585 (3094 by post)	219	455	146
1943	6692	6824 (2831 by post)	138	334	236

The Committee desires to express its thanks to all donors of newly published books, and also to those whose gifts of early volumes have enriched the Society's historical collection.

Several important journals, published in enemy and occupied territory and reproduced by the photo-offset process in the United States of America, have been acquired and have been of considerable use to readers; microfilms of the "Berichte" and "Liebig's Annalen" have been frequently consulted in the Library, as several of these volumes are not obtainable in any other form.

The direct importation of American books has continued satisfactorily, and enabled readers to gain prompt access to many important works.

A further service to readers has been instituted in the issue by the Librarian of vouchers enabling them to borrow volumes from the Science Library.

Members of ten Constituent and Contributing Bodies now use the Library. This number includes the British Association of Chemists to whose members facilities have recently been granted for a provisional period of one year.

The increase in attendances previously referred to has presented serious problems in accommodating readers in comfort. This has been particularly so on Saturday mornings when, during the three hours the Library is open, as many as 35 readers have attended. The maximum number which can be seated to work in comfort is 9, and often it has been necessary to seat 13, whilst others have been compelled to stand. That the Library is still so extensively used, despite all the inconveniences, which include climbing 67 stairs to an overcrowded reading-room, with only a small proportion of the books accessible to readers, stresses the vital importance of the Library. It also serves to indicate what a great service to chemistry could be rendered by the Library were it housed in adequate premises.

APPENDIX C.

LECTURES, ETC., HELD DURING 1944.

Given in London.

20th January, *Tilden Lecture*, "The Scope and Limitations of Infra-red Measurements in Chemistry," by Dr. H. W. Thompson; 17th February. *Lecture*, "Chemotherapy in Tropical Medicine," by Dr. A. J. Ewins; 16th March, *Ninth Pedler Lecture*, "Newer Knowledge of the Biochemistry of the Thyroid Gland," by Dr. C. R. Harington; 18th May, *Tilden Lecture*, "Some Aspects of the Organic Chemistry of Phosphorus and Arsenic," by Dr. F. G. Mann; 19th October, *Tilden Lecture*, "Non-benzenoid Aromatic Hydrocarbons," by Professor Wilson Baker; 16th November, *Meeting* for reading papers.

Given outside London.

Bristol. 13th January, *lecture*, "Post-War Coal Processing," by Mr. G. M. Gill and Mr. J. Roberts; 4th February, *lecture*, "The Thermal Reactions of the Paraffins," by Dr. C. E. H. Bawn; 16th March, *lecture*, "Chemotherapy," by Mr. L. E. H. Whitby; 5th October, *lecture*, "Microchemistry," by Dr. J. K. N. Jones; 2nd November, *lecture*, "Effects of Pollution on Deposits in the Mersey Estuary," by Mr. B. A. Southgate; 7th December, *lecture*, "Ion Exchangers applied to Water Treatment," by Mr. M. R. T. Pemberton. These were joint meetings with the Royal Institute of Chemistry and the Society of Chemical Industry, and were held at the University.

Edinburgh. 11th February, at the University, *lecture,* "Molecular Regimentation in Solid and Liquid," by Professor G. M. Bennett; 7th October, at the University (joint meeting with the Edinburgh University Chemical Society, the Royal Institute of Chemistry, and the Society of Chemical Industry), *lecture,* "Some Aspects of Steroid Metabolism," by Professor G. F. Marrian.

Glasgow. 18th February, at the Royal Technical College, *Tilden Lecture,* "The Scope and Limitations of Infra-red Measurements in Chemistry," by Dr. H. W. Thompson, preceded by the annual general meeting of local Fellows; 17th November, at the Royal Technical College, *lecture,* "The Value of the Resonance Concept in Chemistry," by Mr. R. P. Bell; 27th November, at the Royal Technical College (joint meeting with the Glasgow University Alchemists Club and the Andersonian Chemical Society), *lecture,* "Some Recent Studies in Diazo-Chemistry," by Dr. H. H. Hodgson.

Leeds. 2nd March, at the University (Official Meeting of the Society and joint meeting with the Leeds University Chemical Society), *discussion* on "The Mechanism of Oxidation-Reduction Reactions," opened by Professor H. S. Raper, Professor M. G. Evans, and Dr. W. A. Waters; 9th October, at the University, *lecture,* "Some Trends in Chemical Spectroscopy and the Study of Large Molecules," by Dr. H. W. Thompson.

Liverpool. 13th January, at the University (joint meeting with the Royal Institute of Chemistry, the Society of Chemical Industry and the British Association of Chemists), *lecture,* "The 'Reactivity' of Organic Compounds," by Professor E. D. Hughes; 15th September, at the University (joint meeting with the British Association of Chemists), *lecture,* "Corrosion of Metals in Chemical Plant," by Dr. S. J. Kennett; 12th October, at the University (joint meeting with the Royal Institute of Chemistry), *lecture,* "Sulphur Dioxide-Retrospect and Prospect," by Mr. G. Brearley.

Manchester. 20th January, at the Engineers' Club (joint meeting with the Royal Institute of Chemistry), *lecture,* "Pyrethrum and the Pyrethrins," by Dr. A. E. Gillam; 29th February, at the University, *meeting* for the reading of papers; 24th March, at the University, *Ninth Pedler Lecture,* "Newer Knowledge of the Biochemistry of the Thyroid Gland," by Dr. C. R. Harington; 29th September, at the College of Technology (joint meeting with the Royal Institute of Chemistry), Exhibition of Scientific Films; 8th November, at the University (joint meeting with the Manchester Unversity Chemical Society, and the Royal Institute of Chemistry), *lecture,* "Chemistry in Relation to National Prosperity," by Professor I. M. Heilbron; 19th December, in the Central Library Lecture Hall, *first Dalton lecture,* "Chemistry and Clothing," by Dr. D. Clibbens (joint meeting with the Royal Institute of Chemistry).

Newcastle and Durham. 17th March, at King's College (Official Meeting of the Society), *Tilden Lecture,* "Some Aspects of the Organic Chemistry of Phosphorus and Arsenic," by Dr. F. G. Mann.

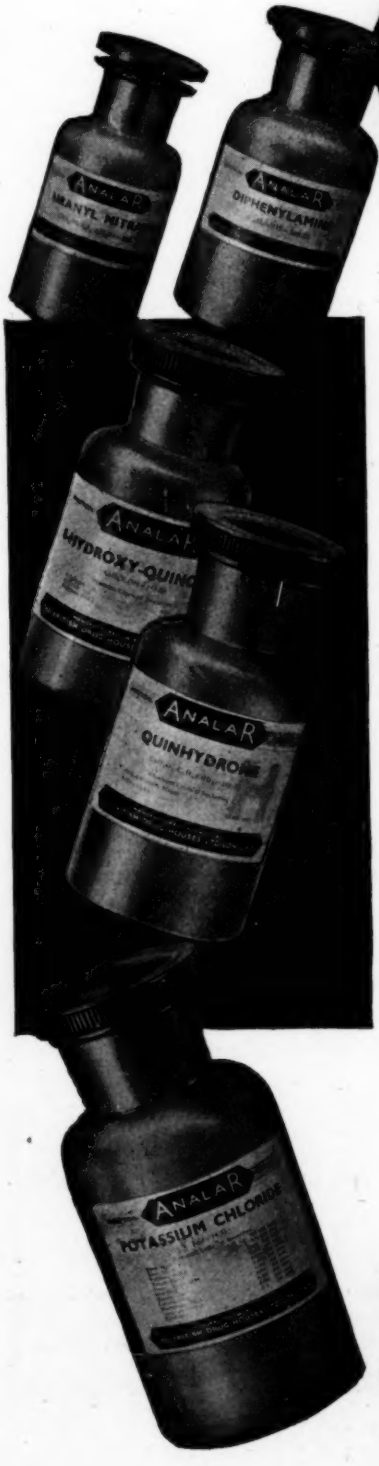
North Wales. 11th February, at University College, Bangor (joint meetings with the University College, Bangor, Chemical Society), "Substitution," by Professor C. K. Ingold; 16th November, *lecture,* "Oxidation of Phenols," by Professor R. D. Haworth.

Nottingham. 28th March, at University College, *lecture,* "Some Aspects of the Organic Chemistry of Phosphorus and Arsenic," by Dr. F. G. Mann; 20th November, at University College, *lecture,* "The Usefulness of the Concept of Resonance in Chemistry," by Mr. R. P. Bell.

Sheffield. 11th February, at the University, *lecture,* "The Synthesis of Chemotherapeutic Agents," by Mr. S. Ellingworth; 12th May, at the University (Official Meeting of the Society), *lecture,* "Carbohydrates Containing Nitrogen and Other Elements," by Professor W. N. Haworth; 1st September, at the University (joint meeting with the University Chemical Society), *lecture,* "The Chemistry of Glass Formation," by Professor W. E. S. Turner; 10th November, at the University (joint meeting with the University Chemical Society), *lecture,* "Co-ordination Compounds," by Professor W. Wardlaw.

South Wales. 21st January, at Technical College, Cardiff (joint meeting with the Cardiff Technical College Chemical Society), *lecture,* "Chemical Reactivity," by Professor E. D. Hughes, *also* given on 22nd January at University College, Swansea (joint meeting with the University College Students Chemical Society); 12th February, at University College, Cardiff (joint meeting with the Royal Institute of Chemistry), *lecture,* "The Study of Reaction Mechanism," by Dr. H. B. Watson; 3rd March, at University College, Cardiff (joint meeting with the Royal Institute of Chemistry and the Society of Chemical Industry), *lecture,* "Enzymes and Vitamins," by Professor A. R. Todd.

Eire. 23rd February, at University College, Dublin (joint meeting with the Royal Institute of Chemistry), *lecture* "Monomolecular Films," by Dr. V. E. J. Davidson.



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